

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: July 16, 2003, 19:29:49 ; Search time 40 Seconds

(without alignments)
721.008 Million cell updates/sec

Title: US-09-935-727-2

Sequence: 1 KRALGPGSLICLVIALPA.....RVARMGLERSVREPLPVH 300

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 283224 seqs, 96134422 residues

Total number of hits satisfying chosen parameters: 283224

Minimum DB seq length: 0
Maximum DB seq length: 200000000

Post-processing: Minimum Match 0%
Maximum Match 100%

Listing first 45 summaries

Database :
1: pir1:*
2: pir2:*
3: pir3:*
4: pir4:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | Query Match | Length | DB | ID | Description |
|------------|-------|-------------|--------|----|--------|--------------------|
| 1 | 351.5 | 21.5 | 461 | 1 | A35356 | tumor necrosis fac |
| 2 | 333.5 | 20.4 | 459 | 2 | I48854 | gene murine tumour |
| 3 | 332.5 | 20.3 | 474 | 2 | B38634 | tumor necrosis fac |
| 4 | 315 | 19.3 | 435 | 2 | I54182 | tumor necrosis fac |
| 5 | 295.5 | 18.1 | 651 | 2 | JC7705 | death receptor-6 - |
| 6 | 262.5 | 16.1 | 349 | 2 | D72175 | G2R protein - Varl |
| 7 | 262.5 | 16.1 | 349 | 2 | D36858 | gene G4R protein - |
| 8 | 262 | 16.0 | 348 | 2 | T28623 | hypothetical prote |
| 9 | 236.5 | 14.5 | 325 | 2 | B43692 | T2 protein - rabbi |
| 10 | 226 | 13.8 | 277 | 2 | I37552 | Ox40 homolog - hum |
| 11 | 215 | 13.2 | 326 | 1 | GOVZML | T2 protein - myxom |
| 12 | 214 | 13.1 | 271 | 1 | SL2783 | Ox40 antigen precu |
| 13 | 211 | 12.9 | 277 | 2 | A60771 | B-cell activation |
| 14 | 203 | 12.4 | 305 | 2 | A46476 | gene oxa4 protein |
| 15 | 198.5 | 12.1 | 272 | 2 | I48700 | B cell-associated |
| 16 | 186.5 | 11.4 | 595 | 2 | A42086 | CD30 antigen precu |
| 17 | 185 | 11.3 | 256 | 2 | B32393 | T-cell antigen 4-1 |
| 18 | 176 | 10.8 | 416 | 1 | JN0006 | nerve growth facto |
| 19 | 175.5 | 10.7 | 427 | 1 | G0HUN | nerve growth facto |
| 20 | 174 | 10.6 | 255 | 2 | I38426 | lymphocyte activat |
| 21 | 170 | 10.4 | 425 | 1 | A26431 | nerve growth facto |
| 22 | 159.5 | 9.8 | 260 | 1 | A46517 | CD27 antigen precu |
| 23 | 155.5 | 9.5 | 327 | 2 | A46484 | apoptosis-mediati |
| 24 | 148.5 | 9.1 | 1574 | 2 | T13954 | MEG6 protein - ra |
| 25 | 148 | 9.1 | 250 | 1 | A49053 | CD27 antigen precu |
| 26 | 147.5 | 9.0 | 5376 | 2 | T42215 | zonadhesin - mouse |
| 27 | 145 | 8.9 | 335 | 2 | A40036 | apoptosis-mediati |
| 28 | 144 | 8.8 | 324 | 2 | JC2395 | Fas antigen precu |
| 29 | 143.5 | 8.8 | 1299 | 2 | T43251 | furin (EC 3.4.21.7 |

| | | | | | | |
|----|-------|-----|------|---|--------|--------------------|
| 30 | 143 | 8.8 | 1620 | 2 | T27283 | hypothetical prote |
| 31 | 140 | 8.6 | 314 | 2 | I37383 | FAS soluble protei |
| 32 | 137.5 | 8.4 | 454 | 1 | G0MST1 | tumor necrosis fac |
| 33 | 135 | 8.3 | 2321 | 2 | S78549 | notch3 protein - h |
| 34 | 133 | 8.1 | 493 | 2 | UC5486 | membrane glycoprot |
| 35 | 129.5 | 7.9 | 1548 | 2 | S34583 | serine proteinase |
| 36 | 128.5 | 7.9 | 3635 | 2 | T10053 | laminin alpha 5 ch |
| 37 | 127 | 7.8 | 1192 | 2 | S69000 | laminin gamma 2 ch |
| 38 | 125.5 | 7.7 | 461 | 1 | G0RPT1 | tumor necrosis fac |
| 39 | 125.5 | 7.7 | 1255 | 1 | A24571 | protein-tyrosine k |
| 40 | 124.5 | 7.6 | 1713 | 2 | A55347 | adhesive ligand ep |
| 41 | 124.5 | 7.6 | 3106 | 1 | S53868 | laminin alpha-2 ch |
| 42 | 123.5 | 7.6 | 455 | 1 | G0HUT1 | tumor necrosis fac |
| 43 | 122.5 | 7.5 | 2824 | 2 | T22759 | hypothetical prote |
| 44 | 120 | 7.3 | 1609 | 1 | MMHNB2 | laminin gamma-1 ch |
| 45 | 120 | 7.3 | 2318 | 2 | S45306 | notch 3 protein - |

ALIGNMENTS

RESULT 1
A35356
tumor necrosis factor receptor 2 precursor [validated] - human
N:Alternate names: 75K tumor necrosis factor receptor; TNF receptor type 2
C:Species: Homo sapiens (man)
C>Date: 10-Sep-1999 #sequence, revision 10-Sep-1999 #text, change 08-Dec-2000
C:Accession: A35356; A36475; A48416; A36007; A23666; B35010; I38094
R:Smith, C.A.; Davis, T.; Anderson, D.; Solam, L.; Beckmann, M.P.; Jerzy, R.; Dower, Science 248, 1019-1023, 1990
A:Title: A receptor for tumor necrosis factor defines an unusual family of cellular A:Reference number: A35356; MIMD:90260639; PMID:2160731
A:Accession: A35356
A>Status: preliminary
A:Molecule type: mRNA
A:Residues: 1-461 <SMI>
A:Cross-references: GB:M32315; NID:q189185; PIDN:AA5929.1; PID:q189186
R:Kohn, T.; Brewer, M.T.; Baker, S.L.; Schwartz, P.E.; King, M.W.; Hale, K.K.; Squir Proc. Natl. Acad. Sci. U.S.A. 87, 8331-8335, 1990
A:Title: A second tumor necrosis factor receptor gene product can shed a naturally oc A:Reference number: A36475; MIMD:91045991; PMID:2172983
A:Accession: A36475
A>Status: preliminary
A:Molecule type: mRNA
A:Residues: 1-195, 'R', 197-461 <KOH>
A:Cross-references: GB:M38549; NID:q339757; PIDN:AA36755.1; PID:q339758
R:Dembic, Z.; Loetscher, H.; Gubler, U.; Pan, Y.C.; Lahm, H.W.; Gentsz, R.; Brockhaus, Cytokine 2, 231-237, 1990
A:Title: Two human TNF receptors have similar extracellular, but distinct intracellular A:Reference number: A48416; MIMD:91370690; PMID:1966549
A:Accession: A48416
A>Status: preliminary
A:Molecule type: mRNA; protein
A:Residues: 23-461 <DEM>
A:Cross-references: GB:S63368; NID:q235648; PIDN:AA19824.1; PID:q235649
A:Note: sequence extracted from NCBI backbone (NCIN:63368, NCBI:P.3371)
R:Keller, R.A.; Song, K.; Onasch, M.A.; Fischer, W.H.; Chang, D.; Ringold, G.M. Proc. Natl. Acad. Sci. U.S.A. 87, 6151-6155, 1990
A:Title: Complementary DNA cloning of a receptor for tumor necrosis factor and demons A:Reference number: A36007; MIMD:90349572; PMID:2166946
A:Accession: A36007
A>Status: preliminary
A:Molecule type: mRNA
A:Residues: 116-140, 'P', 142-195, 'R', 197-362, 'T', 364-461 <HEU>
A:Cross-references: GB:M35857; NID:q339751; PIDN:AA63262.1; PID:q339752
R:Loetscher, H.; Schlaeger, E.J.; Lahm, H.W.; Pan, Y.C.E.; Lesslauer, W.; Brockhaus, J. Biol. Chem. 265, 20131-20138, 1990
A:Title: Purification and partial amino acid sequence analysis of two distinct tumor A:Reference number: A23666; MIMD:91056048; PMID:2173696
A:Accession: A23666
A>Status: preliminary
A:Molecule type: protein
A:Residues: 23-40; 65-69; 136-141; 300-306 <LOE>

R.Engelmann, H.; Novick, D.; Wallach, D.
 J. Biol. Chem. 265, 1531-1536, 1990
 A:Title: Two tumor necrosis factor-binding proteins purified from human urine. Evidence
 A:Reference number: A35010; MUID:90110215; PMID:2153136
 A:Accession: B35010
 A:Status: preliminary
 A:Molecule type: protein
 A:Residues: 27-31 <ENG>
 R.Kuhmert, P.; Kemper, O.; Wallach, D.
 Gene 150, 381-386, 1994
 A:Title: Cloning, sequencing and partial functional characterization of the 5' region of
 A:Reference number: 138094; MUID:95121934; PMID:7821811
 A:Accession: 138094
 A:Status: preliminary; translated from GB/EMBL/DBJ
 A:Molecule type: DNA
 A:Residues: 1-37 <RES>
 A:Cross-references: EMBL:X80021; NID:9666044; PIDN:CAA56324.1; PID:9625701
 C:Genetics:
 A:Gene: GDB:TNR2
 A:Cross-references: GDB:125914; OMIM:191191
 A:Map position: 1p36.2-1p36.2
 A:Introns: 26/3
 A>Note: the list of introns is incomplete
 C:Superfamily: tumor necrosis factor receptor type 2; NGF receptor repeat homology
 C:Keywords: duplication; glycoprotein; receptor; transmembrane protein
 F:1-22/Domain: signal sequence #status predicted <SIS>
 F:23-416/Product: tumor necrosis factor receptor 2 #status experimental <MAT>
 F:40-76/Domain: NGF receptor repeat homology <NG1>
 F:78-119/Domain: NGF receptor repeat homology <NG2>
 F:120-163/Domain: NGF receptor repeat homology <NG3>
 F:164-201/Domain: NGF receptor repeat homology <NG4>
 F:262-279/Domain: transmembrane #status predicted <TMN>
 F:280-461/Domain: intracellular #status predicted <INT>
 F:171.193/Binding site: carbohydrate (Asn) (covalent) #status predicted

Query Match 21.5%; Score 351.5; DB 1; Length 461;
 Best Local Similarity 29.8%; Pred. No. 6.2e-19;
 Matches 96; Conservative 43; Mismatches 122; Indels 61; Gaps 12;

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QY      8 GISTLCLVLPALPVPVAVRGVAVETPYPMRDAETGE-----RLVCAACPPG 55
DB      13 GELMAAAHALPA-----QVAFTPYAP-----EPGSCRRLREYYDQAKCCSKCSFG 60
QY      56 TFVQPCRRDPTTGCPDPRIHYTOPWNYLEKRCRYCNVLCGEREEARACHATHNACRC 115
DB      61 QHAKVCTKTSPTVDCSDCEDSTYTQLMNVVPECLSCGSRCSDDOYETQACTREONRITC 120
QY      116 RTGEFAHNG-----FCLHASCPRGAGVIAAGTFSQNTQCCPPGPGFSASSSSEQC 169
DB      121 RFGWICALSKQPCGCRKLCAPLRKCRPGFVGARPGTETSDVYCKPCAPGTFSTNTSDICR 180
QY      170 PHRNCTALGLNVPSSSHDTLCTGCTGFPLSTFVPGAECEERAVIDFVAFQDISIKRL 229
DB      181 PHQICNVVA-----IGNMSMDAVCTSTS-----PTRSMAPGAVHLPOV-----STRSQHT 227
QY      230 QRLDALAEPE-----GKGPTRPRA-----GRAALQTLKRRRLTELLGADGALLVRLQAL 280
DB      228 QPTPPTAPSTPSFLLPMKPPPAEGSTGDFALPGLIIVGYAL-----GLIIIGVNCV 282
QY      281 ---RVARMP-GLERSVREERFLP 298
DB      283 INTQVKKKPLCLQDREAKVPHLP 304

```

RESULT 2
 148854
 gene murine tumor necrosis factor receptor 2 protein - mouse (fragment)
 C:Species: Mus musculus (house mouse)
 C:Date: 02-Jul-1996 #sequence_revision 02-Jul-1996 #text_change 23-Jul-1999
 C:Accession: 148854
 R.Powell, E.E.; Wicker, L.S.; Peterson, L.B.; Todd, J.A.
 Mamm. Genome 5, 726-727, 1994
 A:Title: Allelic variation of the type 2 tumor necrosis factor receptor gene.

A:Reference number: 148854; MUID:95178848; PMID:7873884
 A:Accession: 148854
 A:Status: preliminary; translated from GB/EMBL/DBJ
 A:Molecule type: mRNA
 A:Residues: 1-459 <RES>
 A:Cross-references: EMBL:X76401; NID:9433830; PIDN:CAA53981.1; PID:9433831
 C:Superfamily: tumor necrosis factor receptor type 2; NGF receptor repeat homology
 F:151-188/Domain: NGF receptor repeat homology <NGF>

Query Match 20.4%; Score 333.5; DB 2; Length 459;
 Best Local Similarity 29.7%; Pred. No. 1.4e-17;
 Matches 81; Conservative 43; Mismatches 110; Indels 39; Gaps 9;

```

QY      46 RLVCACPPGTFVQPCRRDPTTGCPDPRIHYTOPWNYLEKRCRYCNVLCGEREEARAC 105
DB      37 QMCAKCPGQYVKKHFCNKTSPTVCADEASMYTQVMNDFRLCLSCSSSCSDOYETBAC 96
QY      106 HATHNRACRCRTGFE-----AHAGF-----CLEHASCPRGAGVIAAGTFSQNTQCCPPGCTF 158
DB      97 TKQNRNVCACEAGRYCALKTHSGSCQCRILSKCGPGFVAVSRAPNGNVLCACAPGTF 156
QY      159 SASSSSEQCQPHRNCTALGLANVPSSSHDTLCT-----SCTGFPPLSTRVPGAECEBERRA 214
DB      157 SFTTSTDYCRHRILCSILA-----IPGNASTDAVCAPESTLAIPTRIYVSGPEPTNSQ 212
QY      215 VIDVAFDIDISIKRLQRLQLEADPEGWCPPE-----RAGRAALQTLKRRRLTELLGAD 269
DB      213 PLD-----QBPGRSQPISITLSL-----GSTPIIQSTKGTSLPGLIVGTSL----- 257
QY      270 GALLVRLQAL-----RVARMPGLERSVREERFLP 298
DB      258 GLIMLGLVNCFLVQRRKKRPSCLQDQAKVHPV 290

```

RESULT 3
 B38634
 tumor necrosis factor receptor type 2 precursor - mouse
 C:Species: Mus musculus (house mouse)
 C:Date: 30-Jun-1992 #sequence_revision 30-Jun-1992 #text_change 23-Jul-1999
 C:Accession: B38634; A40254; S54816
 R.Lewis, M.; Tartaglia, L.A.; Lee, A.; Bennett, G.L.; Rice, G.C.; Wong, G.H.W.; Chen,
 Proc. Natl. Acad. Sci. U.S.A. 88, 2830-2834, 1991
 A:Title: Cloning and expression of cDNAs for two distinct murine tumor necrosis facto
 A:Reference number: A38634; MUID:91187885; PMID:1849278
 A:Accession: B38634
 A:Molecule type: mRNA
 A:Residues: 1-474 <LEN>
 A:Cross-references: GB:M60469; NID:9199827; PIDN:AAA39752.1; PID:9199828
 R.Goodwin, R.G.; Anderson, D.; Jerzy, R.; Davis, T.; Brannan, C.I.; Copeland, N.G.; J
 Mol. Cell. Biol. 11, 3020-3026, 1991
 A:Title: Molecular cloning and expression of the type 1 and type 2 murine receptors f
 A:Reference number: A40254; MUID:91246168; PMID:1645445
 A:Accession: A40254
 A:Molecule type: mRNA
 A:Residues: 1-474 <GOO>
 A:Cross-references: GB:M60469; NID:9199827; PIDN:AAA39752.1; PID:9199828
 R.Kisnerighis, M.; Fellowes, R.; Feldmann, M.; Chernaiovsky, Y.
 submitted to the EMBL Data Library, May 1995
 A:Description: Characterization of the promoter region of the murine p75-TNF receptor
 A:Reference number: S54816
 A:Accession: S54816
 A:Molecule type: DNA
 A:Status: preliminary
 A:Residues: 1-22 <KIS>
 A:Cross-references: EMBL:X87128; NID:9609043; PIDN:CAA60618.1; PID:9609044
 C:Superfamily: tumor necrosis factor receptor type 2; NGF receptor repeat homology
 C:Keywords: cytokine receptor; transmembrane protein
 F:1-22/Domain: signal sequence #status predicted <SIS>
 F:23-474/Product: tumor necrosis factor receptor type 2 #status predicted <MAT>
 F:40-77/Domain: NGF receptor repeat homology <NG1>
 F:79-120/Domain: NGF receptor repeat homology <NG2>
 F:166-203/Domain: NGF receptor repeat homology <NG4>

| | | | | | | |
|----|-----------------------|---|--------------------|-------|-----------------|-------------------|
| | Query Match | 20.3%; | Score 332.5; | DB 2; | Length 474; | |
| | Best Local Similarity | 29.7%; | Pred. No. 1.7e-17; | | | |
| | Matches | 81; | Conservative | 44; | Mismatches 109; | IndeIs 39; Gaps 9 |
| QY | 46 | RIVACGPPGFHFVORPCRDSPITTCGPCCPRHHYOFNMYLBERCRVCNVLGCEEEAEAC | 105 | | | |
| | : | : :: :: : | : | : | :: : | : |
| Db | 52 | QMCAKCPGGGVYHFNCKNTSDTYCACDEASMTYQWVMQFRTCLSSCSTTDDYEIYAC | 111 | | | |
| QY | 106 | HATHNRACRCRGTFF---AHAGF---CLEHASCPGAGVIAPGTPSONTOQCPCPGTF | 158 | | | |
| | : | : :: :: :: : | : | : | :: : | : |
| Db | 112 | TKGONRVACBAGRICALKTHSGSQRCQMRLSKCGPGEVVASRPANGNLCKACAPGF | 171 | | | |
| QY | 159 | SASSSSSQOCPHNHCIALGLALNVPGSSSHDTICT---SCTGFPDLSRYPGAECERA | 214 | | | |
| | : | : :: :: :: : | : | : | :: : | : |
| Db | 172 | SDTTSSTDVCCRPHRICSLA---IPGNASTDAVCAPESPILSAIPRLYVSQPPEPTRSO | 227 | | | |
| QY | 215 | VIDVFAPODISIKRQLRLOALEAPEGSGPP-----RAGRAIDLKLRRRLTELLGROD | 269 | | | |
| | : | : :: :: :: : | : | : | :: : | : |
| Db | 228 | PLD---OEPPSQPPSLITSL-----GSTPIEQSKTGKISLPILIGLVGTSL----- | 272 | | | |
| QY | 270 | GALLVRLLQAL-----RVARMGLEYSVEREFLP | 298 | | | |
| | : | : :: :: : | : | : | :: : | : |
| Db | 273 | GLMGLGVNCIIIVORKKKPSCLOADAKVAHPVP | 305 | | | |

RESULT 4
154182
tumor necrosis factor receptor 2-related protein - human
C:Species: Homo sapiens (man)
C:Date: 24-May-1996 #sequence_revision 24-May-1996 #text_change 17-Mar-2000
C:Accession: 154182
R:Baens, M.; Chaffanet, M.; Cassiman, J.J.; Van den Berghe, H.; Marynen, P.
Genomics 16, 214-218, 1993
A:Title: Construction and evaluation of a hncDNA library of human 12p transcribed sequences
A:Reference number: 154182; MUID:93252381; PMID:8486360
A:Accession: 154182
A:Status: preliminary; translated from GB/EMBL/DBJ
A:Molecule type: mRNA
A:Residues: 1-435 <RES>
A:Cross-references: GB:I04270; NID:g339761; PIDN:AAA36757.1; PID:g339762
C:Genetics:
A:Gene: GDB:ITBR
A:Cross-references: GDB:1230195; OMIM:600979
A:Map position: 12p13.3-12p13.1
A:Superfamily: tumor necrosis factor receptor type 1; NGF receptor repeat homology.

| | | | | |
|-----------------------|-------|--------------------|-------|-------------------------------------|
| Query Match | 19.3% | Score 315; | DB 2; | Length 435; |
| Best Local Similarity | 31.8% | Pred. No. 3.1e-16; | | |
| Matches | 89; | Conservative | 29; | Mismatches 120; Indels 42; Gaps 12. |

| | | | | | |
|----|-----|---------------------------------------|----------------------------------|-------------|-----|
| QY | 3 | ALEGGISLLCLVIALPALPVPVAVRGVAETPTV---- | PWRDA----- | ETGERLVCACQ | 52 |
| | | : | : | : | : |
| Db | 6 | ATSAAPGAMGLVIGLFGILLAASQPAV--- | PYPASENOTORDDEKEYEEOHRIACCRC | | 62 |
| QY | 53 | PGAFVOPRCRRDSPTCGPCPRPHIYDFMYVL-- | ERCRCYNVLCGREGEPARCAHTH | | 109 |
| | | : | : | : | : |
| Db | 63 | PGRTYVSAKCKRINDYVATCAENSYNNHMYLTICQ | LCRCRDPMG-- | LEEIACPTSKR | 120 |
| QY | 110 | NRACRCRTGFPAHAGFCLF--H---- | ASCPGGA-GVIAPGPSONTQCCPCPGTESASS | | 162 |
| | | : | : | : | : |
| Db | 121 | KTGRCRQGMFC-AAMALECTHCELLSCCPGTEALE | LDDEYKGNHCVPCAKGHFQNTS | | 179 |
| QY | 163 | SSSECCOPHRNCTALGILANPGSSSHDTLCTSCG | FLSTRVPAECCEBAVIDFVAFQ | | 222 |
| | | : | : | : | : |
| Db | 180 | SPSARQCPHTCEMGLVEAPAGTAQSDPTTCKNPLE | -PLPEPMSTMLMLAVLLPLAPFL | | 238 |
| QY | 223 | DIS----- | IKRLORLLQALEAPGSGFTTPRAG | | 249 |
| | | ::: | ::: | ::: | ::: |
| Db | 239 | LLATVFSCIMKSHPSLCKRIKSLIK--RRQDEG | ENPAPAG | | 276 |

RESULT 5
JC7705

death receptor-6 - chicken
C:Species: Gallus gallus (chicken)
C:Date: 09-Nov-2001 #sequence_revision 09-Nov-2001 #text_change 09-Nov-2001
C:Accession: Jc7705
R:Bridgeham, J.T.; Bobe, J.; Goeltz, F.W.; Johnson, A.L.
Biochem. Biophys. Res. Commun. 284, 1109-1115, 2001
A:Title: Conservation of death receptor-6 in avian and piscine vertebrates.
A:Reference number: Jc7705; MUID:21308433; PMID:11414698
A:Accession: Jc7705
A:Molecule type: mRNA
A:Residues: 1-651 <BRI>
A:Cross-references: GB:AF349908
C:Comment: This receptor, a member of the tumor necrosis factor receptor family, belongs to the TNF receptor superfamily and is involved in the regulation of cell death and/or survival signaling cascade.
C:Genetics:
A:Gene: dr-6
C:Keywods: ovary
F:1-1/Domain: signal sequence #status predicted <SIG>
F:52-196/Domain: extracellular cysteine-rich, ligand-binding #status predicted <ECCL>
F:333-350/Domain: transmembrane #status predicted <TM>
F:410-475/Domain: death domain #status predicted <ED>
F:551-651/Region: conserved cytoplasmic #status predicted

| | | | | |
|-----------------------|-------|-------------------|-----------|---------------|
| Query Match | 18.1% | Score 295.5 | DB 2 | Length 651 |
| Best Local Similarity | 30.8% | Pred. No. 1,3e-14 | | |
| Matches | 61 | Conservative | 30 | Mismatches 92 |
| | | | Indels 15 | Gaps 1 |

| | | | | |
|----|-----|---|----------------------------|----|
| QY | 18 | LPAALPYPAVARGVAETP----- | TYPRDAETGERLVCAQCPGPTGVQRC | 62 |
| | | : | | |
| | | : | | |
| Db | 6 | LAVALPLVFGTADAOPLKTSQONAAVSLPAGKYLHLDRATQOELICDKCPGTVSKHC | 65 | |
| | | : | | |
| | | : | | |
| QY | 63 | RDSPTTGCPCPRHYYTOFMVYLERCRVNCVLCGEREEARCAHTTHRACRCRTGFPAH | 122 | |
| | | : | | |
| | | : | | |
| Db | 66 | TKSTLRECSPCPDGFTFTHENGIEKCHCRKPCLEPLMEIKTHCTALTYDRECLLSGTQOI | 125 | |
| | | : | | |
| | | : | | |
| QY | 123 | AGFCLLEHAASCPGAGVIAIPGPSONTQOCPCPPGTFSSASSSSSEDCQPHRNCTALGLAIN | 182 | |
| | | : | | |
| | | : | | |
| Db | 126 | NDTQVPLPYVACPEVGMGVRKGTETEDYRCKPCLRGFTFSDVPSSVMKCKTYTDCFGKRMVYV | 185 | |
| | | : | | |
| | | : | | |
| QY | 183 | VPSSSHDTLCTSCGFP | 200 | |
| | | : | | |
| | | : | | |
| Db | 186 | KPGTKESDNNVXSPASLP | 203 | |
| | | : | | |
| | | : | | |

RESULT 6
D72175
G2R protein - variola minor virus (strain Garcia-1966)
C:Species: variola minor virus
C:Date: 24-Nov-1999 #sequence.revision 24-Nov-1999 #text.change 20-Jun-2000
C:Accession: D72175
R:Shehelkunov, S.N.; Tolmenin, A.V.; Gutorov, V.V.; Safonov, P.F.; Massung, R.F.; Lo
submitted to Genbank, March 1998.
A:Description: Analysis of the complete coding sequence of DNA of alastrim variola m
A:Reference number: A72150
A:Accession: D72175
A:Status: Preliminary
A:Molecule type: DNA
A:Residues: 1-349 <SHC>
A:Cross-references: GB:Y16780; NID:q5830555; PIDN:CAB54798.1; PID:q5830759
A:Experimental source: strain Garcia-1966
C:Genetics:
A:Gene: G2R
C:Superfamily: myxoma virus T2 protein; NGF receptor repeat homology

| | | | | | |
|-----------------------|--------|---|---------------|------------|------|
| Query Match | Score | 262.5; | DB 2; | Length | 349; |
| Best Local Similarity | 16.1%; | Pred. | No. 2, 1e-12; | | |
| Matches | 62; | Conservative | 29; | Mismatches | 103; |
| | | | | Indels | 13; |
| | | | | Gaps | 3 |
| OY | 9 | LSLICVIALPALLPVPAVRGVAEPYTPYPMRAETGEGELVLCACGPGPTGQPCRRDST | 68 | | |
| | | | | | |
| Db | 10 | LFLSTIIINGRADAPYTPPENGKCKOTEY-----KRHNLCCTSCSPGYTASMLCDSKITVT | 63 | | |
| OY | 69 | TCGDCPPRHYYQFMWYLERCRKCNVLGCEREEDAPACHATNHRACRCRTGPF-----AH | 122 | | |

```

Db      64 QCTPGSGGFTSRNNHLPALCLSCNGRCNSNOVETRESCNTTHNRICSCSPGYCLLKGSSG 123
QY      123 AGFCLHASCPGAGVIAPCTPSQNTQCCPCPGTFSASSSSSEOCOPHRNCTALGLALN 182
Db      124 CRKACVSQTKGIGYGV-SGHTSVGDVICSRCGCGTGYTSYTSADKCEPVNNTFNIVDE 182
QY      183 VPGSSSHDTLCTSCGTGFPPLSTRVPGA 209
Db      183 ITLYPVNDTSCRTTGTGLESILTSE 209

RESULT 7
D36858
gene G4R protein - variola virus
N:Alternate names: B28R protein (COP)
C:Species: variola virus
C>Date: 30-Sep-1993 #sequence_revision 30-Sep-1993 #text_change 23-Mar-2001
C:Accession: D36858; S46888; S32385; S35987
R:Blinov, V.M.
submitted to GenBank, November 1992
A:Reference number: A36859
A:Accession: D36858
A:Status: preliminary
A:Molecule type: DNA
A:Residues: 1-349 <BLI>
A:Cross-references: GB:X69198; NID:9456758; PIDN:CAA49137.1; PID:9457087
A:Experimental source: strain Indla-1967, isolate Ind3
R:Kolyhalov, A.A.; Blinov, V.M.; Gyorov, V.V.; Pozdnyakov, S.G.; Chizhikov, V.E.; Frolo
submitted to the EMBL Data Library, April 1992
A:Description: Nucleotide sequence analysis of the region of variola virus xhoI F O H P
A:Reference number: S46888
A:Accession: S46888
A:Status: preliminary
A:Molecule type: DNA
A:Residues: 1-349 <KOL>
A:Cross-references: EMBL:X67117; NID:9516428; PIDN:CAA47540.1; PID:9516449
A:Experimental source: strain Indla-1967, isolate Ind3
R:Shchelkunov, S.N.; Blinov, V.M.; Sandakhchilev, L.S.
FEBS Lett. 319, 80-83, 1993
A:Title: Genes of variola and vaccinia viruses necessary to overcome the host protective
A:Reference number: S32385; MUID:93202281; PMID:8384129
A:Accession: S32385
A:Molecule type: DNA
A:Residues: 31-168 <SHC>
A:Cross-references: EMBL:X69198
A:Experimental source: strain Indla-1967, ssp. major
C:Genetics:
A:Gene: G4R
C:Superfamily: myxoma virus T2 protein; NGF receptor repeat homology
F:32-66/Domain: NGF receptor repeat homology <NGF>
F:58-109/Domain: NGF receptor repeat homology <NG2>
F:110-151/Domain: NGF receptor repeat homology <NG3>

Query Match      16.1%; Score 262.5; DB 2; Length 349;
Best Local Similarity 30.0%; Pred. No. 2.1e-12;
Matches 62; Conservative 29; Mismatches 103; Indels 13; Gaps 3;

QY      9 LSLCLVALPALPAPVAVGVAETPTYPWRDAETGERLVCAQCPGTFVQRCRRDSP 68
Db      10 LFLSCIIINGRDAAPTPPNCKCKTET-----KRNHLCCLSCPGTYSRLCDSKTIN 63
QY      69 TCGPCPPRHYYTOFWNYLERCRVCNVLGGEREEARACHATHNRACRCRTGFF-----AH 122
Db      64 OCTPGSGGFTSRNNHLPALCLSCNGRCNSNOVETRESCNTTHNRICSCSPGYCLLKGSSG 123
QY      123 AGFCLHASCPGAGVIAPCTPSQNTQCCPCPGTFSASSSSSEOCOPHRNCTALGLALN 182
Db      124 CRKACVSQTKGIGYGV-SGHTSVGDVICSRCGCGTGYTSYTSADKCEPVNNTFNIVDE 182
QY      183 VPGSSSHDTLCTSCGTGFPPLSTRVPGA 209
Db      183 ITLYPVNDTSCRTTGTGLESILTSE 209

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RESULT 8
T28623
hypothetical protein G2R - variola major virus
C:Species: variola major virus
C>Date: 22-Oct-1999 #sequence_revision 22-Oct-1999 #text_change 21-Jul-2000
C:Accession: T28623
R:Massung, R.F.; Esposito, J.J.; Liu, L.I.; Qi, J.; Ulteback, T.R.; Knight, J.C.; Au
Nature 366, 748-751, 1993
A:Title: Potential virulence determinants in terminal regions of variola smallpox vir
A:Reference number: Z20488; MUID:94088747; PMID:8264798
A:Accession: T28623
A:Status: preliminary; translated from GB/EMBL/DDBJ
A:Molecule type: DNA
A:Residues: 1-348 <MAS>
A:Cross-references: EMBL:L22579; NID:9623595; PIDN:AAA60933.1; PID:9439102
A:Experimental source: strain Bangladesh 1975
C:Superfamily: myxoma virus T2 protein; NGF receptor repeat homology

Query Match      16.0%; Score 262; DB 2; Length 348;
Best Local Similarity 30.8%; Pred. No. 2.3e-12;
Matches 64; Conservative 28; Mismatches 100; Indels 16; Gaps 4;

QY      9 LSLCLVALPALPAPVAVGVAETPTYPWRDAETGERLVCAQCPGTFVQRCRRDSP 67
Db      10 LFLSCIIINGRDAAPTPPNCKCKTETPTYPWRDAETGERLVCAQCPGTFVQRCRRDSP 61
QY      68 TTGCGPCPPRHYYTOFWNYLERCRVCNVLGGEREEARACHATHNRACRCRTGFF-----A 121
Db      62 TQCTPGSGGFTSRNNHLPALCLSCNGRCNSNOVETRESCNTTHNRICSCSPGYCLLKGSS 121
QY      122 HAFCLHASCPGAGVIAPCTPSQNTQCCPCPGTFSASSSSSEOCOPHRNCTALGLALN 181
Db      122 GCKACVSQTKGIGYGV-SGHTSVGDVICSRCGCGTGYTSYTSADKCEPVNNTFNIVDE 180
QY      182 NVPSSSHDTLCTSCGTGFPPLSTRVPGA 209
Db      181 EITLYPVNDTSCRTTGTGLESILTSE 208

RESULT 9
B43692
T2 protein - rabbit fibroma virus
C:Species: rabbit fibroma virus, Shope fibroma virus
C>Date: 30-Sep-1993 #sequence_revision 30-Sep-1993 #text_change 07-May-1999
C:Accession: B43692
R:Upton, C.; Delange, A.M.; McFadden, G.
Virology 160, 20-30, 1987
A:Title: Tumorigenic poxviruses: genomic organization and DNA sequence of the telomer
A:Reference number: A43692; MUID:87321103; PMID:2820128
A:Accession: B43692
A:Status: preliminary
A:Molecule type: DNA
A:Residues: 1-325 <OPT>
A:Cross-references: GB:M17433
C:Superfamily: myxoma virus T2 protein; NGF receptor repeat homology
F:64-105/Domain: NGF receptor repeat homology <NG2>
F:106-147/Domain: NGF receptor repeat homology <NG3>

Query Match      14.5%; Score 236.5; DB 2; Length 325;
Best Local Similarity 29.9%; Pred. No. 1.7e-10;
Matches 58; Conservative 25; Mismatches 94; Indels 17; Gaps 4;

QY      11 LCLVALPALPAPVAVGVAETPTYPWRDAETGERLVCAQCPGTFVQRCRRDSP 70
Db      8 LVCVVYVDDVDPVYSSNOGCGGHDY-----EKDGLCASCHPGGTFYASRLCGPGSNVVC 61
QY      71 GPCPPRHYYTOFWNYLERCRVCNVLGGEREEARACHATHNRACRCRTGFFA-----HAG 124
Db      62 SPEDGTFYASRNHAACVSCRCPCGTHLSSESQPCRTIHDRCNCSTGNYCLLKGNGCR 121
QY      125 FCLHASCPGAGVIAPCTPSQNTQCCPCPGTFSASSSSSEOCOPHRNCTALGLALNP 184

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Db 122 ICAPQTKCPAGYGV-SGHTRAGDTLCEKCPKPTHTYSLSPTFRCGTSFNVISVGFNL--- 177
 QY 185 GSSSHDTLCTSGT 198
 Db 178 -YPVNETSCTTTAG 190

RESULT 10

137552
 OX40 homolog - human
 C:Species: Homo sapiens (man)
 C>Date: 29-May-1998 #sequence_revision 29-May-1998 #text_change 11-Jan-2000
 C:Accession: 137552
 R:Latza, U.; Dutkop, H.; Schlittner, S.; Ringeling, J.; Eitelbach, F.; Hummel, M.; Fonat
 Eur. J. Immunol. 24, 677-683, 1994
 A:Title: The human OX40 homolog: cDNA structure, expression and chromosomal assignment
 A:Reference number: 137552; MUID:94170844; PMID:7510240
 A:Accession: 137552
 A:Status: preliminary; translated from GB/EMBL/DBJ
 A:Molecule type: mRNA
 A:Residues: 1-277 <RES>
 A:Cross-References: EMBL:X75962; NID:g472957; PIDN:CAA53576.1; PID:g472958
 C:Superfamily: CD27 antigen; NGF receptor repeat homology

Query Match 13.8%; Score 226; DB 2; Length 277;
 Best Local Similarity 27.0%; Pred. No. 8.9e-10;
 Matches 80; Conservative 25; Mismatches 117; Indels 74; Gaps 12;

QY 6 GFGSLICLVIALPALLPVAVRGVAETPTYPWRDAETGERLYCAOCPGTFVORPCRD 65
 Db 11 GPCALLLLGLSLSTVTLGHCV-----GDTYPSNR-----CCHCRGNGMVSCHS 59
 QY 66 SPTTGCPRPRIYTOFWNT--LERCRYCNVLCGEREEERACHATNRACRGTGFANA 123
 Db 60 QNTVCRPCGPGFYNDVSSKPCPCPCWCMIRSG--SERQLTATQDTVCRCRAG----- 112
 QY 124 GFCLEHASCPPGAGVIAPGTPSQNTQCPCPGTFSSSSSSPCOPHNCTALGLANV 183
 Db 113 --TQPLDSYKRG-----YDCACPCPGHF--SGDNDACPCPWNCTLAGHITQ 156
 QY 184 PGSSSHDTLCTG--CTGFPPLSTRVPGAECEERAVIDFAVDISIKRLQLALEAPE 240
 Db 157 PASNSDAICEDRDPATQPOETGPPAPPI-----TVQPRE 193
 QY 241 GW-----GTPPR-----AGRALQLKRRRLTELLGAOGALLVRLQLARVAMP 286
 Db 194 AMPRTSQGPSTRPEVPGGRAVAAILGLVGLGLPL--ATLALYLLRRDQRLP 247

RESULT 11

GOVZML
 T2 protein - myxoma virus (strain Lausanne)
 C:Species: myxoma virus
 C>Date: 31-Dec-1992 #sequence_revision 31-Dec-1992 #text_change 18-Jun-1999
 C:Accession: A40566
 R:Upjohn, C.; Macen, J.L.; Schreiber, M.; Mcfadden, G.
 Virology 184, 370-382, 1991
 A:Title: Myxoma virus expresses a secreted protein with homology to the tumor necrosis
 A:Reference number: A40566; MUID:91335768; PMID:1651597
 A:Accession: A40566
 A:Molecule type: DNA
 A:Residues: 1-326 <PPT>
 A:Cross-References: GB:M95181; GB:M37976; NID:g332309; PIDN:AAA46632.1; PID:g332310
 C:Superfamily: myxoma virus T2 protein; NGF receptor repeat homology
 C:Keywords: glycoprotein
 F:64-105/Domain: NGF receptor repeat homology <NG3>
 F:106-147/Domain: NGF receptor repeat homology <NG3>
 F:66,181,205,238/Binding site: carbohydrate (Asn) (covalent) #status predicted

Query Match 13.2%; Score 215; DB 1; Length 326;
 Best Local Similarity 29.3%; Pred. No. 6.9e-09;
 Matches 58; Conservative 22; Mismatches 96; Indels 22; Gaps 5;

QY 12 LCVIALPALP-----PVPVAVRGVAETPTYPWRDAETGERLYCAOCPGTFVORPCRD 66
 Db 4 LFTLLAVACVYGGGAPYADRGKRGNDY-----ERGLCTSCPPSSYARLCPGS 57
 QY 67 PTTCGCPRPRIYTOFWNT--LERCRYCNVLCGEREEERACHATNRACRGTGFANA 121
 Db 58 DTVCSPCKNETFTASTNHAPACVSCRCRGTGLHSESQCDKTRDVCDCSAGNYCLKQ 117
 QY 122 -HAGFLEHASCPPGAGVIAPGTPSQNTQCPCPGTFSSSSSSPCOPHNCTALGLA 180
 Db 118 EGCRIAPYTKCPAGYGV-SGHTRAGDTLCTCRPRYTDAYSSTETCTSSFNVISVEPN 176
 QY 181 LWPVGSSSHDTLCTSGT 198
 Db 177 L-----YPVNDISCTTTAG 190

RESULT 12

S12783
 OX40 antigen precursor - rat
 N:Alternate names: nerve growth factor receptor homolog
 C:Species: Rattus norvegicus (Norway rat)
 C>Date: 30-Sep-1993 #sequence_revision 30-Sep-1993 #text_change 05-Nov-1999
 C:Accession: S12783; S08036
 R:Mallett, S.; Fossum, S.; Barclay, A.N.
 EMBO J. 9, 1063-1068, 1990
 A:Title: Characterization of the MRC OX40 antigen of activated CD4 positive T lymphoc
 A:Reference number: S12783; MUID:90214614; PMID:2157591
 A:Accession: S12783
 A:Molecule type: mRNA
 A:Residues: 1-271 <MAL>
 A:Cross-References: EMBL:X17037; NID:g57830; PIDN:CAA34897.1; PID:g57831
 C:Superfamily: CD27 antigen; NGF receptor repeat homology
 C:Keywords: growth factor receptor; transmembrane protein
 F:1-19/Domain: signal sequence #status predicted <Sig>
 F:20-271/Product: OX40 antigen #status predicted <Mat>
 F:211-235/Domain: transmembrane #status predicted <TM>

Query Match 13.1%; Score 214; DB 2; Length 271;
 Best Local Similarity 30.1%; Pred. No. 6.9e-09;
 Matches 58; Conservative 23; Mismatches 64; Indels 48; Gaps 9;

QY 10 SLICLVIALPALLPVAVRGVAETPTYPWRDAETGERLYCAOCPGTFVORPCRDSPPT 69
 Db 10 AFLILSLIGVYKLCVK-----DTYP-----SGHK--CCRECPHGMVSRCDHRTDY 58
 QY 70 CGCPRPRIYTOFWNT--LERCRYCNVLCGEREEERACHATNRACRGTGFANAFCFL 127
 Db 59 CHPCGPGFYNEAVNYDTCKQCTQCNHRS--SELKQNCPTEDTVQC----- 105
 QY 128 EHASCPPGAGVIAPGT-PSQNT-----QCPCPGTFSSSSSSPCOPHNCTALGLA 180
 Db 106 -----PGTPRODSHKLGVDCVPCPGHF--SPGSNOACKPWNCTLSGKQ 150
 QY 181 LWPVGSSSHDTLCT 193
 Db 151 IRHPASNSLDTVC 163

RESULT 13

A60771
 B-cell activation protein CD40 precursor - human
 N:Alternate names: B-cell surface antigen Bp50
 C:Species: Homo sapiens (man)
 C>Date: 03-Jun-1993 #sequence_revision 03-Feb-1994 #text_change 21-Jul-2000
 C:Accession: S04460; A60771
 R:Stamenkovic, I.; Clark, E.A.; Seed, B.
 EMBO J. 8, 1403-1410, 1989
 A:Title: A B-lymphocyte activation molecule related to the nerve growth factor recept
 A:Reference number: S04460; MUID:89356508; PMID:2475341
 A:Accession: S04460
 A:Molecule type: mRNA

GenCore version 5.1.6
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OW protein - protein search, using sw model

Run on: July 16, 2003, 19:39:49 ; Search time 19 Seconds
(without alignments)
1517.912 Million cell updates/sec

Title: US-09-935-727-2

Perfect score: 300

Sequence: 1 MRALRPGSLSLCLVIALPA.....RYARMPLGERSVEREFLPVH 300

Scoring table:

Gapop 60.0 , Gapext 60.0

Searched: 283224 seqs, 96134422 residues

Word size: 0

Total number of hits satisfying chosen parameters: 283224

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Listing first 45 summaries

Database:

PIR_73:*
1: pir1:*
2: pir2:*
3: pir3:*
4: pir4:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | Query Match | Length | DB ID | Description |
|------------|-------|-------------|--------|-------|-------------|
| 1 | 9 | 3.0 | 327 | 2 | H83483 |
| 2 | 9 | 3.0 | 561 | 2 | H84800 |
| 3 | 8 | 2.7 | 179 | 1 | KGR |
| 4 | 8 | 2.7 | 181 | 2 | T49104 |
| 5 | 8 | 2.7 | 184 | 2 | I49685 |
| 6 | 8 | 2.7 | 191 | 2 | G90670 |
| 7 | 8 | 2.7 | 191 | 2 | C85521 |
| 8 | 8 | 2.7 | 241 | 2 | T05479 |
| 9 | 8 | 2.7 | 297 | 2 | AH0341 |
| 10 | 8 | 2.7 | 341 | 2 | T27654 |
| 11 | 8 | 2.7 | 440 | 2 | T50912 |
| 12 | 8 | 2.7 | 494 | 1 | S60028 |
| 13 | 8 | 2.7 | 494 | 2 | AD0751 |
| 14 | 8 | 2.7 | 530 | 2 | F90893 |
| 15 | 8 | 2.7 | 530 | 2 | C85124 |
| 16 | 8 | 2.7 | 530 | 2 | B64905 |
| 17 | 8 | 2.7 | 531 | 1 | S54098 |
| 18 | 8 | 2.7 | 644 | 2 | JC5119 |
| 19 | 8 | 2.7 | 781 | 2 | T49472 |
| 20 | 8 | 2.7 | 1172 | 1 | TSHRP2 |
| 21 | 7 | 2.3 | 26 | 1 | B57082 |
| 22 | 7 | 2.3 | 27 | 1 | S07443 |
| 23 | 7 | 2.3 | 27 | 1 | SEBO |
| 24 | 7 | 2.3 | 27 | 1 | SESH |
| 25 | 7 | 2.3 | 27 | 2 | A27267 |
| 26 | 7 | 2.3 | 27 | 2 | C60415 |
| 27 | 7 | 2.3 | 56 | 2 | A95855 |
| 28 | 7 | 2.3 | 57 | 2 | C84255 |
| 29 | 7 | 2.3 | 74 | 2 | S13515 |

| | | | | | | |
|----|---|-----|-----|---|--------|--------------------|
| 30 | 7 | 2.3 | 87 | 2 | G85063 | hypothetical prote |
| 31 | 7 | 2.3 | 89 | 2 | S13517 | retinoic acid rece |
| 32 | 7 | 2.3 | 106 | 2 | G82729 | hypothetical prote |
| 33 | 7 | 2.3 | 112 | 2 | G72502 | hypothetical prote |
| 34 | 7 | 2.3 | 113 | 1 | IMECE1 | colicin EI immunit |
| 35 | 7 | 2.3 | 113 | 2 | I64785 | imm protein - Esch |
| 36 | 7 | 2.3 | 113 | 2 | S11532 | colicin EI immunit |
| 37 | 7 | 2.3 | 114 | 2 | S44660 | ZK353.5 protein - |
| 38 | 7 | 2.3 | 118 | 2 | S27476 | hypothetical prote |
| 39 | 7 | 2.3 | 131 | 1 | SEBG | secretin precursor |
| 40 | 7 | 2.3 | 133 | 2 | JC2202 | secretin precursor |
| 41 | 7 | 2.3 | 134 | 2 | A40959 | secretin precursor |
| 42 | 7 | 2.3 | 140 | 2 | T27059 | hypothetical prote |
| 43 | 7 | 2.3 | 140 | 2 | C72705 | hypothetical prote |
| 44 | 7 | 2.3 | 144 | 1 | TVVPBD | small T antigen - |
| 45 | 7 | 2.3 | 150 | 2 | S34380 | hypothetical prote |

ALIGNMENTS

RESULT 1

H83483

probable transmembrane sensor PA1301 [Imported] - Pseudomonas aeruginosa (strain PA01)

C:Species: Pseudomonas aeruginosa

C>Date: 15-Sep-2000 #sequence_revision 15-Sep-2000 #text_change 15-Jun-2001

C:Accession: H83483

R:Stover, C.K.; Pham, X.Q.; Erwin, A.L.; Mizoguchi, S.D.; Warren, P.; Hickey, M.J.;

adman, S.; Yuan, Y.; Brody, L.L.; Coulter, S.N.; Folger, K.R.; Kas, A.; Larbig, K.; L

.; Lory, S.; Olson, M.V.

Nature 406, 959-964, 2000

A>Title: Complete genome sequence of Pseudomonas aeruginosa PA01, an opportunistic pa

A:Reference number: AB2950, M01D:20437337, PMID:10984043

A:Accession: H83483

A>Status: preliminary

A:Molecule type: DNA

A:Residues: 1-327 <STO>

A:Cross-references: GB:AE004559; GB:AE004091; NID:g9947228; PIDN:AMG04690.1; GSPDB:GN

A:Experimental source: strain PA01

C:Genetics:

A:Gene: PA1301

C:Superfamily: Pseudomonas putida regulatory protein pupR

Query Match

Best Local Similarity 3.0%; Score 9; DB 2; Length 327;

Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 16 LALPALPV 24

Db 304 LALPALPV 312

RESULT 2

D84800

hypothetical protein At2g38060 [Imported] - Arabidopsis thaliana

C:Species: Arabidopsis thaliana (mouse-ear cress)

C>Date: 02-Feb-2001 #sequence_revision 02-Feb-2001 #text_change 02-Feb-2001

C:Accession: D84800

R:Lin, X.; Kaul, S.; Rounsley, S.D.; Shea, T.P.; Benito, M.I.; Town, C.D.; Fujii, C.Y

M.; Koo, H.; Moffat, K.S.; Cronin, L.A.; Shen, M.; VanAken, S.E.; Umayam, L.; Tallon,

euss, D.; Nieman, W.C.; White, O.; Eisen, J.A.; Salzberg, S.L.; Fraser, C.M.; Venter

Nature 402, 761-768, 1999

A>Title: Sequence and analysis of chromosome 2 of the plant Arabidopsis thaliana.

A:Reference number: AB4420; M01D:20083467; PMID:10617197

A:Accession: D84800

A>Status: preliminary

A:Molecule type: DNA

A:Residues: 1-561 <STO>

A:Cross-references: GB:AE002093; NID:g4895179; PIDN:AAD32766.1; GSPDB:GN00139

C:Genetics:

A:Gene: At2g38060

A:Map position: 2

Query Match 3.0%; Score 9; DB 2; Length 561;
 Best Local Similarity 100.0%; Pred. No. 2.5;
 Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 6 GPGSLI.LCL 14
 DB 405 GPGSLI.LCL 413

RESULT 3

KCRT

gamma-casein precursor - rat

C:Species: Rattus norvegicus (Norway rat)

C:Date: 13-Jun-1983 #sequence_revision 13-Jun-1983 #text_change 31-May-1996

C:Accession: A03111

R:Hobbs, A.A.; Rosen, J.M.

Nucleic Acids Res. 10, 8079-8098, 1982

A:Title: Sequence of rat alpha- and gamma-casein mRNAs: evolutionary comparison of the c

A:Reference number: A93452; MUID: 83143278; PMID: 6298707

A:Accession: A03111

A:Molecule type: mRNA

A:Residues: 1-179 <HOB>

C:Superfamily: gamma-casein

C:Keywords: phosphoprotein

F:1-15/Domain: signal sequence #status predicted <SIG>

F:16-179/Product: gamma-casein #status predicted <MAT>

Query Match 2.7%; Score 8; DB 1; Length 179;
 Best Local Similarity 100.0%; Pred. No. 8.4;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 159 SASSSSSE 166
 DB 50 SASSSSSE 57

RESULT 4

T49104

hypothetical protein AT4g21970 - Arabidopsis thaliana

C:Species: Arabidopsis thaliana (mouse-ear cress)

C:Date: 02-Jun-2000 #sequence_revision 02-Jun-2000 #text_change 02-Jun-2000

C:Accession: T49104

R:Bayan, M.; Medler, H.; Wandut, R.; Bancroft, I.; Mewes, H.W.; Rudd, S.; Lemcke, K.; M

submitted to the Protein Sequence Database, May 2000

A:Reference number: Z25016

A:Accession: T49104

A:Status: preliminary

A:Molecule type: DNA

A:Residues: 1-181 <BEV>

A:Cross-references: EMBL:AL022140; GSPDB:GN00062; ATSP:AT4g21970

A:Experimental source: cultivar Columbia; BAC clone FIN20

C:Genetics: A:Gene: ATSP:AT4g21970

A:Map position: 4

A:introns: 142/1

Query Match 2.7%; Score 8; DB 2; Length 181;
 Best Local Similarity 100.0%; Pred. No. 8.4;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 158 FSASSSSS 165
 DB 35 FSASSSSS 42

RESULT 5

I49685

gamma-casein precursor - mouse

C:Species: Mus musculus (house mouse)

C:Date: 02-Aug-1996 #sequence_revision 02-Aug-1996 #text_change 13-Aug-1999

C:Accession: I49685

R:Sasaki, T.; Sasaki, M.; Enami, J.

Zool. Sci. 10, 65-72, 1993

A:Title: Mouse gamma-casein cDNA: PCR cloning and sequence analysis.

A:Reference number: I49685; MUID: 93320737; PMID: 7763793

A:Accession: I49685

A:Status: preliminary; translated from GB/EMBL/DBJ

A:Molecule type: mRNA

A:Residues: 1-184 <RES>

A:Cross-references: GB:D10215; NID:g220404; PIDN:BA01067.1; PID:g220405

C:Superfamily: gamma-casein

Query Match 2.7%; Score 8; DB 2; Length 184;
 Best Local Similarity 100.0%; Pred. No. 8.6;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 159 SASSSSSE 166
 DB 51 SASSSSSE 58

RESULT 6

G90670

probable oxidoreductase ECs0335 [imported] - Escherichia coli (strain O157:H7, substr

C:Species: Escherichia coli

C:Date: 18-Jul-2001 #sequence_revision 18-Jul-2001 #text_change 18-Jul-2001

C:Accession: G90670

R:Hayashi, T.; Makino, K.; Ohnishi, M.; Kurokawa, K.; Ishii, K.; Yokoyama, K.; Han, C

gasawara, N.; Yasunaga, T.; Kuhara, S.; Shiba, T.; Hattori, M.; Shinagawa, H.

DNA Res. 8, 11-22, 2001

A:Title: Complete genome sequence of enterohemorrhagic Escherichia coli O157:H7 and 9

A:Reference number: A96629; MUID: 21156231; PMID: 11258796

A:Accession: G90670

A:Status: preliminary

A:Molecule type: DNA

A:Residues: 1-191 <HAY>

A:Cross-references: GB:BA000007; PIDN:BA833758.1; PID:g13359792; GSPDB:GN00154

A:Experimental source: strain O157:H7, substrain RMD 0509952

C:Genetics: A:Gene: ECs0335

Query Match 2.7%; Score 8; DB 2; Length 191;
 Best Local Similarity 100.0%; Pred. No. 8.8;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 210 ECERAVID 217
 DB 27 ECERAVID 34

RESULT 7

C85521

probable oxidoreductase ECs0335 [imported] - Escherichia coli (strain O157:H7, substr

C:Species: Escherichia coli

C:Date: 16-Feb-2001 #sequence_revision 16-Feb-2001 #text_change 27-Nov-2001

C:Accession: C85521

R:Perna, N.T.; Plunkett III, G.; Burland, V.; Mau, B.; Glasner, J.D.; Rose, D.J.; May

Miller, L.; Grothbeck, E.J.; Davis, N.W.; Lim, A.; Diallanita, E.; Potamousis, K.; Apoda

Nature 409, 529-533, 2001

A:Title: Genome sequence of enterohemorrhagic Escherichia coli O157:H7.

A:Reference number: A85480; MUID: 21074935; PMID: 11206551

A:Accession: C85521

A:Status: preliminary

A:Molecule type: DNA

A:Residues: 1-191 <STO>

A:Cross-references: GB:AB005174; NID:g12513095; PIDN:AA654631.1; GSPDB:GN00145; UWGP:

A:Experimental source: strain O157:H7, substrain EDL933

C:Genetics: A:Gene: Z0374

Query Match 2.7%; Score 8; DB 2; Length 191;
 Best Local Similarity 100.0%; Pred. No. 8.8;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 210 ECERAVID 217
 DB 27 ECERAVID 34

Db 27 ECERAVID 34

RESULT 8

T05479 hypothetical protein T805.180 - Arabidopsis thaliana

C:Species: Arabidopsis thaliana (mouse-ear cress)

C>Date: 23-Apr-1999 #sequence_revision 23-Apr-1999 #text_change 23-Jul-1999

C:Accession: T05479

R:Revan, M.; Wedler, H.; Wambitt, R.; Bancroft, I.; Mewes, H.W.; Mayer, K.F.X.; Schueller submitted to the Protein Sequence Database, February 1998

A:Reference number: Z15417

A:Accession: T05479

A:Molecule type: DNA

A:Residues: 1-241 <BEV>

A:Cross-references: EMBL:AL021890

A:Experimental source: cultivar Columbia; BAC clone T805

C:Genetics:

A:Map position: 4

A:Introns: 142/1; 169/3; 193/1; 211/1; 223/3

A>Note: T805.180

Query Match

Best Local Similarity 100.0%; Pred. No. 11;

Matches 8; Conservative 0; Indels 0; Gaps 0;

OY 158 FSASSSS 165

Db 35 FSASSSS 42

RESULT 9

AH0341

Probable aldo/keto reductase (EC 1.1.1.-) [imported] - Versinia pestis (strain CO92)

C:Species: Versinia pestis

C>Date: 02-Nov-2001 #sequence_revision 02-Nov-2001 #text_change 27-Nov-2001

C:Accession: AH0341

R:Parkhill, J.; Wren, B.W.; Thomson, N.R.; Titball, R.W.; Holden, M.T.G.; Prentice, M.B.; den-Raaij, A.M.; Chillingworth, T.; Cronin, A.; Davies, R.M.; Davis, P.; Dougan, G.;

11. M.; Rutherford, K.; Simmonds, M.; Skelton, J.; Stevens, K.; Whitehead, S.; Barrett, Nature 413, 523-527, 2001

A>Title: Genome sequence of Versinia pestis, the causative agent of plague.

A:Reference number: AB0001; M0ID:21470413; PMID:11586360

A:Accession: AH0341

A>Status: preliminary

A:Molecule type: DNA

A:Residues: 1-297 <KUR>

A:Cross-references: GB:AL590842; PIDN:CAC93039.1; PID:G15980777; GSPDB:GN00175

C:Genetics:

A:Gene: YPO2805

C:Superfamily: aldehyde reductase

C:Keywords: oxidoreductase

Query Match

Best Local Similarity 100.0%; Pred. No. 13;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 210 ECERAVID 217

Db 41 ECERAVID 48

RESULT 10

T27654

hypothetical protein ZK1025.9 - Caenorhabditis elegans

C:Species: Caenorhabditis elegans

C>Date: 15-Oct-1999 #sequence_revision 15-Oct-1999 #text_change 15-Oct-1999

C:Accession: T27654

R:Lennard, N. submitted to the EMBL Data Library, March 1998

A:Reference number: Z20400

A:Accession: T27654

A>Status: preliminary; translated from GB/EMBL/DBJ

A:Molecule type: DNA

A:Residues: 1-341 <NTL>

A:Cross-references: EMBL:AL022288; PIDN:CAA18368.1; GSPDB:GN00019; CESP:ZK1025.9

A:Experimental source: clone ZK1025

C:Genetics:

A:Gene: CESP:ZK1025.9

A:Map position: 1

A:Introns: 6/1; 54/1; 76/1; 97/1; 158/3; 232/2; 324/3

Query Match

Best Local Similarity 100.0%; Pred. No. 15;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 159 SASSSSE 166

Db 103 SASSSSE 110

RESULT 11

T50912

hypothetical protein ORF440 [imported] - Rubrivivax gelatinosus

C:Species: Rubrivivax gelatinosus

C>Date: 21-Jul-2000 #sequence_revision 21-Jul-2000 #text_change 21-Jul-2000

C:Accession: T50912

R:Nagashima, K.V.; Igarashi, N.; Harada, J.; Nagashima, S.; Matsura, K.; Shimada, K. submitted to the EMBL Data Library, November 1999

A:Description: Determination of Nucleotide Sequences of Rubrivivax gelatinosus Photos

A:Reference number: Z25270

A:Accession: T50912

A>Status: preliminary; translated from GB/EMBL/DBJ

A:Molecule type: DNA

A:Residues: 1-440 <NAG>

A:Cross-references: EMBL:AB034704; PIDN:BA04065.1

A:Experimental source: strain IL144

C:Genetics:

A>Note: ORF440

Query Match

Best Local Similarity 100.0%; Pred. No. 18;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 16 LALPALLP 23

Db 42 LALPALLP 49

RESULT 12

S60028

ferredoxin-NADP reductase (EC 1.18.1.2) precursor - mouse

C:Species: Mus musculus (house mouse)

C>Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 03-Jun-2002

C:Accession: S60028; I49671

R:Itoh, S.; Iemura, O.; Yamada, E.; Yoshimura, T.; Tsujikawa, K.; Kohana, Y.; Minura, Biochim. Biophys. Acta 1264, 159-162, 1995

A>Title: cDNA cloning of mouse ferredoxin reductase from kidney.

A:Reference number: I49671; M0ID:96085117; PMID:7495857

A:Accession: S60028

A:Molecule type: mRNA

A:Residues: 1-494 <ITO>

A:Cross-references: EMBL:DA9920; NID:G1088468; PIDN:BAA08659.1; PID:G1088469

C:Genetics:

A:Genome: nuclear

C:Superfamily: human ferredoxin-NADP+ reductase

C:Keywords: FAD; mitochondrion; NADP; oxidoreductase

F;1-34/Domain: transit peptide (mitochondrion) #status predicted <TMP>

F;35-494/Product: ferredoxin-NADP+ reductase #status predicted <MAT>

Query Match

Best Local Similarity 100.0%; Pred. No. 20;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 258 RRRITTELL 265

Db 11111111

Db 276 RRRLELL 283

RESULT 13

AD0751

Cytoplasmic alpha-amylose [imported] - Salmonella enterica subsp. enterica serovar Typhi

A:Species: Salmonella enterica subsp. enterica serovar Typhi

A:Note: this species has also been called Salmonella typhi

C:Date: 09-Nov-2001 #sequence_revision 09-Nov-2001 #text_change 27-Nov-2001

C:Accession: AD0751

R:Parkhill, J.; Dougan, G.; James, K.D.; Thomson, N.R.; Pickard, D.; Main, J.; Churcher, T.; Connor, P.; Cronin, A.; Davis, P.; Davies, R.M.; Dowd, L.; White, N.; Farrar, S.; Moule, S.; O'Gaora, P.

Nature 413, 848-852, 2001

A:Authors: Parry, C.; Quail, M.; Rutherford, K.; Simmonds, M.; Skelton, J.; Stevens, K.

A:Title: Complete genome sequence of a multiple drug resistant Salmonella enterica serov

A:Reference number: AB0502; PMID:11677608

A:Accession: AD0751

A:Status: preliminary

A:Molecule type: DNA

A:Residues: 1-494 <PAR>

A:Cross-references: GB:AL513382; PIDN:CAD05711.1; PID:g16503204; GSPDB:GN00176

C:Genetics:

A:Gene: STY2171

C:Superfamily: alpha-amylose, amyloidquefaciens type; alpha-amylose core homology

Query Match

2.7%; Score 8; DB 2; Length 494;

Best Local Similarity 100.0%; Pred. No. 20;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 232 LLOALEAP 239

DB 335 LLOALEAP 342

RESULT 14

F90893

Probable kinase [imported] - Escherichia coli (strain O157:H7, substrain RIMD 0509952)

C:Species: Escherichia coli

C:Date: 18-Jul-2001 #sequence_revision 18-Jul-2001 #text_change 24-Aug-2001

C:Accession: F90893

R:Haysht, T.; Makino, K.; Ohnishi, M.; Kurokawa, K.; Ishii, K.; Yokoyama, K.; Han, C.G.

gasawara, N.; Yasunaga, T.; Kuhara, S.; Shiba, T.; Hattori, M.; Shinagawa, H.

DNA Res. 8, 11-22, 2001

A:Title: Complete genome sequence of enterohemorrhagic Escherichia coli O157:H7 and gene

A:Reference number: A99629; MUID:21156231; PMID:11258796

A:Accession: F90893

A:Status: preliminary

A:Molecule type: DNA

A:Residues: 1-530 <HAY>

A:Cross-references: GB:BA000007; PIDN:BA035541.1; PID:g13361584; GSPDB:GN00154

A:Experimental source: strain O157:H7, substrain RIMD 0509952

C:Genetics:

A:Gene: ECS2118

C:Superfamily: xylulokinase

Query Match

2.7%; Score 8; DB 2; Length 530;

Best Local Similarity 100.0%; Pred. No. 21;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 41 AETGERLV 48

DB 475 AETGERLV 482

RESULT 15

C85724

Probable kinase ydey [imported] - Escherichia coli (strain O157:H7, substrain EDL933)

C:Species: Escherichia coli

C:Date: 16-Feb-2001 #sequence_revision 16-Feb-2001 #text_change 14-Sep-2001

C:Accession: C85724

R:Perna, N.T.; Plunkett III, G.; Burland, V.; Mau, B.; Glasner, J.D.; Rose, D.J.; Mayhew

Iller, L.; Grobeck, E.J.; Davis, N.W.; Lim, A.; Dimantanta, E.; Potamoussis, K.; Apodaca,

Nature 409, 529-533, 2001

A:Title: Genome sequence of enterohemorrhagic Escherichia coli O157:H7.

A:Reference number: AB5480; MUID:21074935; PMID:11206551

A:Accession: C85724

A:Status: preliminary

A:Molecule type: DNA

A:Residues: 1-530 <STO>

A:Cross-references: GB:AE005174; NID:g12515155; PIDN:AG56255.1; GSPDB:GN00145; UWGP:

A:Experimental source: strain O157:H7, substrain EDL933

C:Genetics:

A:Gene: ydey

C:Superfamily: xylulokinase

Query Match

2.7%; Score 8; DB 2; Length 530;

Best Local Similarity 100.0%; Pred. No. 21;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 41 AETGERLV 48

DB 475 AETGERLV 482

Search completed: July 16, 2003, 19:42:25
Job time : 21 secs

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: July 16, 2003, 19:26:08 ; Search time 23 Seconds

(without alignments)
540,996 Million cell updates/sec

Title: US-09-935-727-2
Perfect score: 1634
Sequence: 1 MRALBPGSLICLVLAIPA.....RVARMPGLERSVREPLPVH 300

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 112892 seqs, 41476328 residues
Total number of hits satisfying chosen parameters: 112892

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SwissProt_40:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | Query Match | Length | ID | Description |
|------------|-------|-------------|--------|---------------|---------------------|
| 1 | 1634 | 100.0 | 300 | 1 TR6B_HUMAN | G95407 homo sapien |
| 2 | 444 | 27.2 | 401 | 1 T11B_HUMAN | O00300 homo sapien |
| 3 | 425.5 | 26.0 | 401 | 1 T11B_RAT | O08727 rattus norv |
| 4 | 424.5 | 26.0 | 401 | 1 T11B_MOUSE | O08712 mus musculu |
| 5 | 351.5 | 21.5 | 461 | 1 TR1B_HUMAN | P20333 homo sapien |
| 6 | 332.5 | 20.3 | 474 | 1 TR1B_MOUSE | P25119 mus musculu |
| 7 | 315 | 19.3 | 435 | 1 TR1B_HUMAN | P36941 mus musculu |
| 8 | 291.5 | 17.8 | 655 | 1 TR21_MOUSE | O95609 mus musculu |
| 9 | 287 | 17.6 | 655 | 1 TR21_HUMAN | O75509 mus musculu |
| 10 | 287 | 17.0 | 415 | 1 TR3_MOUSE | P50284 mus musculu |
| 11 | 262.5 | 16.1 | 349 | 1 CRMB_VARY | P34015 variola vir |
| 12 | 261.5 | 16.0 | 349 | 1 CRMB_CAMPS | Q8uyar camelipox vi |
| 13 | 258.5 | 15.8 | 351 | 1 CRMB_COMPOX | O73559 compox viru |
| 14 | 246 | 15.1 | 283 | 1 TR14_HUMAN | O92956 homo sapien |
| 15 | 239 | 14.6 | 616 | 1 TR11_HUMAN | O95606 homo sapien |
| 16 | 236.5 | 14.5 | 325 | 1 TR11_MOUSE | P25943 Shope fibro |
| 17 | 233.5 | 14.3 | 625 | 1 TR11_MOUSE | O35305 mus musculu |
| 18 | 226 | 13.8 | 277 | 1 TR4_HUMAN | P43489 homo sapien |
| 19 | 215 | 13.2 | 326 | 1 VT2_MYXV | P29825 myxoma viru |
| 20 | 214 | 13.1 | 271 | 1 TR4_RAT | P15725 rattus norv |
| 21 | 211 | 12.9 | 277 | 1 TR5_HUMAN | P25942 homo sapien |
| 22 | 203 | 12.4 | 289 | 1 TR5_MOUSE | P27512 mus musculu |
| 23 | 202 | 12.4 | 269 | 1 TR5_BOVIN | Q28203 bos taurus |
| 24 | 198.5 | 12.1 | 272 | 1 TR4_MOUSE | P47741 mus musculu |
| 25 | 186.5 | 11.4 | 595 | 1 TR8_HUMAN | P28908 homo sapien |
| 26 | 185 | 11.3 | 256 | 1 TR9_MOUSE | P20334 mus musculu |
| 27 | 182.5 | 11.2 | 180 | 1 TR2_MOUSE | O9662 mus musculu |
| 28 | 176 | 10.8 | 416 | 1 TR16_CHICK | P18519 gallus galli |
| 29 | 175.5 | 10.7 | 427 | 1 TR16_HUMAN | P08138 homo sapien |
| 30 | 174 | 10.6 | 235 | 1 TR9_HUMAN | Q07011 homo sapien |
| 31 | 170 | 10.4 | 425 | 1 TR16_RAT | P07174 rattus norv |
| 32 | 167.5 | 10.3 | 176 | 1 TR3_MOUSE | O9663 mus musculu |
| 33 | 166 | 10.2 | 417 | 1 TR16_MOUSE | Q920w1 mus musculu |

ALIGNMENTS

| RESULT 1 | TR6B_HUMAN | STANDARD: | PRT: | 300 AA. |
|----------|---|-----------|------|---------|
| AC | O95407: | | | |
| DT | 15-JUN-2002 (Rel. 41, Created) | | | |
| DT | 15-JUN-2002 (Rel. 41, Last sequence update) | | | |
| DT | 15-JUN-2002 (Rel. 41, Last annotation update) | | | |
| DE | Tumor necrosis factor receptor superfamily member 6B precursor (Decoy receptor for Fas ligand) (Decoy receptor 3) (DCR3) (M68). | | | |
| CN | TNFRSF6B OR DCR3 OR TR6. | | | |
| OS | Homo sapiens (Human). | | | |
| OC | Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi; | | | |
| OC | Mammalia; Eutheria; Primates; Catarrhini; Homiidae; Homo. | | | |
| OX | NCBI_TaxID=9606; | | | |
| RN | [1] | | | |
| RP | SEQUENCE FROM N.A. | | | |
| RC | TISSUE=Fetal lung; | | | |
| RX | MEDLINE=99087326; PubMed=9872321; | | | |
| RA | Pittli R.M., Marsters S.A., Lawrence D.A., Roy M., Kischkel F.C., | | | |
| RA | Dowd P., Huang A., Donahue C.J., Sherwood S.W., Baldwin D.T., | | | |
| RA | Godowski P.J., Wood W.T., Gurney A.L., Hillan K.J., Cohen R.L., | | | |
| RA | Goddard A.D., Botstein D., Ashkenazi A.; | | | |
| RT | "Genomic amplification of a decoy receptor for Fas ligand in lung and | | | |
| RT | colon cancer."; | | | |
| RL | Nature 396:699-703(1998). | | | |
| RN | [2] | | | |
| RP | SEQUENCE FROM N.A., AND SEQUENCE OF 30-35. | | | |
| RC | TISSUE=Prostate; | | | |
| RX | MEDLINE=99253915; PubMed=10318773; | | | |
| RA | Yu K.-Y., Kwon B., Ni J., Zhai Y., Ebner R., Kwon B.S.; | | | |
| RT | "A newly identified member of tumor necrosis factor receptor | | | |
| RT | superfamily (TR6) suppresses LIGHT-mediated apoptosis."; | | | |
| RL | J. Biol. Chem. 274:13733-13736(1999). | | | |
| RN | [3] | | | |
| RP | SEQUENCE FROM N.A. | | | |
| RC | TISSUE=Lung; | | | |
| RX | MEDLINE=20122600; PubMed=10655513; | | | |
| RA | Bai C., Connolly B., Metzger M.L., Hilliard C.A., Liu X., Sandig V., | | | |
| RA | Soderman A., Galloway S.M., Liu Q., Austin C.P., Caskey C.T.; | | | |
| RT | "Overexpression of M68/DCR3 in human gastrointestinal tract tumors | | | |
| RT | independent of gene amplification and its location in a four-gene | | | |
| RL | cluster."; | | | |
| RL | Proc. Natl. Acad. Sci. U.S.A. 97:1230-1235(2000). | | | |
| RP | [4] | | | |
| RP | SEQUENCE FROM N.A. | | | |
| RA | Matthews L.; | | | |
| RL | Submitted (NOV-2000) to the EMBL/GenBank/DBJ databases. | | | |
| RN | [5] | | | |
| RP | SEQUENCE FROM N.A. | | | |
| RC | TISSUE=Lung; | | | |
| RA | Strausberg R.; | | | |
| RL | Submitted (NOV-2001) to the EMBL/GenBank/DBJ databases. | | | |
| CC | -I- FUNCTION: Decoy receptor for the cytotoxic ligands TNFSF14/LIGHT | | | |
| CC | and TNFSF6/FasL. Protects against apoptosis. | | | |
| CC | -I- SUBCELLULAR LOCATION: Secreted. | | | |
| CC | -I- TISSUE SPECIFICITY: Detected in fetal lung, brain and liver. | | | |

| | | | | | | |
|----|-------|------|------|---|------------|--------------------|
| 34 | 163 | 10.0 | 332 | 1 | TNR6_PIG | O77736 sus scrofa |
| 35 | 160.5 | 9.8 | 471 | 1 | TR1A_BOVIN | O19131 bos taurus |
| 36 | 155.5 | 9.5 | 260 | 1 | TNR6_HUMAN | P26842 homo sapien |
| 37 | 135.5 | 9.5 | 327 | 1 | TNR6_MOUSE | P25446 mus musculu |
| 38 | 155 | 9.5 | 323 | 1 | TNR6_BOVIN | P51867 bos taurus |
| 39 | 153 | 9.4 | 241 | 1 | TR18_HUMAN | O9545 homo sapien |
| 40 | 152.5 | 9.3 | 430 | 1 | TR1T_MACFA | O9n092 macaca fasc |
| 41 | 151.5 | 9.3 | 430 | 1 | TR1T_HUMAN | O96924 homo sapien |
| 42 | 148 | 9.1 | 250 | 1 | TNR7_MOUSE | P41272 mus musculu |
| 43 | 147.5 | 9.0 | 5376 | 1 | ZAN_MOUSE | O88799 mus musculu |
| 44 | 147 | 9.0 | 1581 | 1 | LMG3_MOUSE | Q970b6 mus musculu |
| 45 | 145 | 8.9 | 335 | 1 | TNR6_HUMAN | P25445 homo sapien |

CC Detected in adult stomach, spinal cord, lymph node, trachea,
 CC spleen, colon and lung. Highly expressed in several primary tumors
 CC from colon, stomach, rectum, esophagus and in SW480 colon
 CC carcinoma cells.
 CC -1- SIMILARITY: CONTAINS 4 TNFR-CYS REPEATS.
 CC -----
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 CC -----
 DR EMBL: AF104419; AAD03056.1; -
 DR EMBL: AF134240; AAD29688.1; -
 DR EMBL: AF217796; AAF35244.1; -
 DR EMBL: AF217793; AAF33685.1; -
 DR EMBL: AF217794; AAF33686.1; -
 DR EMBL: AL121845; CAC03668.1; -
 DR EMBL: BC017065; AAH17065.1; -
 DR Genew; HGNC:11921; TNFRSF6B.
 DR HSSP: 014763; 1D0G
 DR InterPro: IPR001368; TNFR_c6.
 DR Pfam: PF00020; TNFR_c6; 4.
 DR ProDom: PD000771; TNFR_c6; 1.
 DR SMART: SM00208; TNFR_3.
 DR PROSITE: PS00652; TNFR_NGFR_1; 2.
 DR PROSITE: PS50050; TNFR_NGFR_2; 2.
 DR KMW Receptor; Apoptosis; Glycoprotein; Repeat; Signal.
 FT SIGNAL 1 29
 FT CHAIN 30 300
 FT REPEAT 31 70
 FT REPEAT 72 113
 FT REPEAT 115 150
 FT REPEAT 152 193
 FT DISULFID 49 62
 FT DISULFID 52 70
 FT DISULFID 73 88
 FT DISULFID 91 105
 FT DISULFID 95 113
 FT DISULFID 115 126
 FT DISULFID 132 150
 FT DISULFID 153 168
 FT DISULFID 174 193
 FT CARBOHYD 173 173
 SQ SEQUENCE 300 AA: 32679 MW: P90MEB3718449AF CRC64;
 Query Match 100.0%; Score 1634; DB 1; Length 300;
 Best Local Similarity 100.0%; Pred. No. 6,7e-120;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

RESULT 2
 ID T11B HUMAN STANDARD; PRT; 401 AA.
 AC 000300; 060236; Q9UHP4;
 DT 15-JUN-2002 (Rel. 41, Created)
 DT 15-JUN-2002 (Rel. 41, Last sequence update)
 DT 15-JUN-2002 (Rel. 41, Last annotation update)
 DE Tumor necrosis factor receptor superfamily member 11B precursor
 DE (osteoprotegerin) (osteoclastogenesis inhibitory factor).
 GN TNFRSF11B OR OPB OR OCIF.
 OS Homo sapiens (human).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Homiidae; Homo.
 OX NCBI_TaxID=9606;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE-Kidney;
 RX MEDLINE=97262071; PubMed=9108485;
 RA Simonet W.S., Lacey D.L., Dunstan C.R., Kelley M., Chang M.-S.,
 RA Luethy R., Nguyen H.O., Wooden S., Bennett L., Boone T., Shimamoto G.,
 RA Davy E., Bucay N., Renshaw-Gegg L., Hughes T.M., Hill D., Pattison W.,
 RA Campbell P., Sander S., Van G., Tarpley J., Dery P., Lee R.,
 RA Suggs S., Boyle W.J.;
 RT "Osteoprotegerin: a novel secreted protein involved in the regulation
 RT of bone density.";
 RL Cell 89:309-319(1997).
 RN [2]
 RP SEQUENCE FROM N.A.
 RC TISSUE-Lung cancer;
 RX MEDLINE=98151033; PubMed=9492069;
 RA Yasuda H., Shima N., Nakagawa N., Mochizuki S.-I., Yano K., Fujise N.,
 RA Sato Y., Goto M., Yamaguchi K., Kuriyama M., Kanno F., Murakami A.,
 RA Tsuda E., Morinaga T., Higashio K.;
 RT "Identity of osteoclastogenesis inhibitory factor (OCIF) and
 RT osteoprotegerin (OPG): a mechanism by which OPG/OCIF inhibits
 RT osteoclastogenesis in vitro.";
 RL Endocrinology 139:1329-1337(1998).
 RN [3]
 RP SEQUENCE FROM N.A., AND VARIANT ASN-3.
 RC TISSUE-Placenta;
 RX MEDLINE=98351569; PubMed=9688283;
 RA Morinaga T., Nakagawa N., Yasuda H., Tsuda E., Higashio K.;
 RT "Cloning and characterization of the gene encoding human
 RT osteoprotegerin/osteoclastogenesis-inhibitory factor.";
 RL Eur. J. Biochem. 254:685-691(1998).
 RN [4]
 RP SEQUENCE FROM N.A., AND VARIANT ASN-3.
 RC TISSUE-Eye;
 RA Strausberg R.;
 RL Submitted (MAY-2002) to the EMBL/GenBank/DBJ databases.
 RN [5]
 RP SEQUENCE OF 22-36 AND 378-401.
 RX MEDLINE=98238645; PubMed=9571159;
 RA Tomoyasu A., Goto M., Fujise N., Mochizuki S.-I., Yasuda H.,
 RA Morinaga T., Tsuda E., Higashio K.;
 RT "Characterization of monomeric and homodimeric forms of
 RT osteoclastogenesis inhibitory factor.";
 RL Biochem. Biophys. Res. Commun. 245:382-387(1998).
 RN [6]
 RP SEQUENCE OF 22-393 FROM N.A.
 RC TISSUE-Placenta;
 RA He Z.-Y., Yang G.-Z., Zhang W.-J., Wu X.-F.;
 RT "Cloning and expression of osteoprotegerin from Homo sapiens.";
 RL Acta Biochim. Biophys. Sin. 31:680-684(1999).
 RN [7]
 RP SEQUENCE OF 242-255; 354-359 AND 369-378, AND FUNCTION.
 RX MEDLINE=97312536; PubMed=9168977;
 RA Tsuda E., Goto M., Mochizuki S.-I., Yano K., Kobayashi F.,
 RA Morinaga T., Higashio K.;
 RT "Isolation of a novel cytokine from human fibroblasts that

RT specifically inhibits osteoclastogenesis.";
 RL Biochem. Biophys. Res. Commun. 234:137-142(1997).
 RN [8]
 RP TRAIL BINDING.
 RX MEDLINE-98269100; PubMed-9603945;
 RA Emery J.G., McDonnell P., Burke M.B., Deen K.C., Lyn S., Silverman C.,
 RA Dul E., Appelbaum E.R., Eichman C., DiPintzio R., Dadds R.A.,
 RA James I.E., Rosenberg M., Lee J.C., Young P.R.;
 RT Osteoprotegerin is a receptor for the cytotoxic ligand TRAIL.";
 RL J. Biol. Chem. 273:14363-14367(1998).
 RN [9]
 RP CHARACTERIZATION, AND MUTAGENESIS OF CYS-400.
 RX MEDLINE-98148058; PubMed-9478964;
 RA Yamaguchi K., Kinosaki M., Goto M., Kobayashi F., Tsuda E.,
 RA Morinaga T., Higashio K.;
 RT Characterization of structural domains of human osteoclastogenesis
 RT inhibitory factor.";
 RL J. Biol. Chem. 273:5117-5123(1998).
 RN [10]
 RP REVIEW.
 RX MEDLINE-21395914; PubMed-11505389;
 RA Hofbauer L.C., Neubauer A., Heufelder A.E.;
 RT Receptor activator of nuclear factor-kappaB ligand and
 RT osteoprotegerin: potential implications for the pathogenesis and
 RT treatment of malignant bone diseases.";
 RL Cancer 92:460-470(2001).
 CC -1- FUNCTION: Acts as decoy receptor for RANKL and thereby neutralizes
 CC its function in osteoclastogenesis. Inhibits the activation of
 CC osteoclasts and promotes osteoclast apoptosis in vitro. Bone
 CC homeostasis seems to depend on the local RANKL/OPG ratio. May also
 CC play a role in preventing arterial calcification. May act as decoy
 CC receptor for TRAIL and protect against apoptosis. TRAIL binding
 CC blocks the inhibition of osteoclastogenesis.
 CC -1- SUBUNIT: Homodimer.
 CC -1- SUBCELLULAR LOCATION: Secreted.
 CC -1- TISSUE SPECIFICITY: Highly expressed in adult lung, heart, kidney,
 CC liver, spleen, thymus, prostate, ovary, small intestine, thyroid,
 CC lymph node, trachea, adrenal gland, testis, and bone marrow.
 CC Detected at very low levels in brain, placenta and skeletal
 CC muscle. Highly expressed in fetal kidney, liver and lung.
 CC -1- INDUCTION: Upregulated by increasing calcium concentration in the
 CC medium and estrogens. Downregulated by glucocorticoids.
 CC -1- PTM: N-glycosylated. Contains sialic acid residues.
 CC -1- PTM: N-terminus may be blocked.
 CC -1- SIMILARITY: CONTAINS 4 TNFR-CYS REPEATS.
 CC -1- SIMILARITY: CONTAINS 2 DEATH DOMAINS.
 CC -----
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 CC -----
 DR EMBL: U94332; AAB53709.1; -;
 DR EMBL: AB002146; BAA25910.1; -;
 DR EMBL: AB008822; BAA32076.1; -;
 DR EMBL: AB008821; BAA32076.1; JOINED.
 DR EMBL: BC030155; AAH30155.1; -;
 DR EMBL: AF134187; AAF20168.1; -;
 DR HSSP: P25942; ICDF.
 DR HSPW: HGNC:11909; TNFRSF11B.
 DR MIM: 602643; -;
 DR InterPro: IPR000488; Death.
 DR InterPro: IPR001368; TNFR_c6.
 DR Pfam: PF00020; TNFR_c6; 3.
 DR ProDom: PD000771; TNFR_c6; 1.
 DR SMART: SM00005; DEATH; 1.
 DR SMART: SM00208; TNFR; 4.
 DR PROSITE: PSS0017; DEATH_DOMAIN; FALSE_NEG.
 DR PROSITE: PSS0052; TNFR_NGFR_1; 2.
 DR PROSITE: PSS0050; TNFR_NGFR_2; 2.

KW Receptor; Apoptosis; Glycoprotein; Repeat; Signal; Polymorphism.
 FT SIGNAL 1 21
 FT CHAIN 22 401
 FT
 FT REPEAT 24 62
 FT REPEAT 65 105
 FT REPEAT 107 142
 FT REPEAT 145 185
 FT REPEAT 198 269
 FT DOMAIN 270 365
 FT SITE 400 400
 FT DISULFID 41 54
 FT DISULFID 44 62
 FT DISULFID 65 80
 FT DISULFID 83 97
 FT DISULFID 87 105
 FT DISULFID 107 118
 FT DISULFID 124 142
 FT DISULFID 145 160
 FT DISULFID 166 185
 FT CARBOHYD 98 98
 FT CARBOHYD 152 152
 FT CARBOHYD 165 165
 FT CARBOHYD 178 178
 FT CARBOHYD 289 289
 FT VARIANT 3 3
 FT
 FT MUTAGEN 400 400
 FT MUTAGEN 400 401
 FT CONFLICT 263 263
 FT
 SQ SEQUENCE 401 AA; 46040 MW; EDFA48B67D86C71E CRC64;
 Query Match 27.28; Score 444; DB 1; Length 401;
 Best Local Similarity 39.68; Pred. No. 1.7e-27;
 Matches 84; Conservative 32; Mismatches 86; Indels 10; Gaps 4;

QY 11 LCLVLVALPALLPVPAVGAET--PYPMRDAETGERLYCAACPGTFVQRCRRDSP 68
 DB 4 LLLCAL--VELDISIKWTQETFPFRLHYDETSIQLLDCPCPETIYKONCTAWKT 60
 QY 69 TCGCPRRHYTQFWNTLERCRYCNVLCGEREEARACHATHNRACRCRTGFFAHGCL 128
 DB 61 VCAPCPHYVTDSWHTSDECLYCSPCKELQYQKQECNRYHNRVCEKEGRYLEIEFCLK 120
 QY 129 HASCPEAGVIACTPSONOCPCPGTSSASSSESCOPHNCTALGLALNVPSSS 188
 DB 121 HRSCPPEGVVQGTPEKNTVCKRCPPGPFSSNETSKAPCKKHTNCSVFLLTKGNAT 180
 QY 189 HDTLCTSGTGFPLSTRVGAEE--CERAVIDF 218
 DB 181 HDNI---CSGNSSTQKCGIDVTLCEAFRRF 209
 RESULT 3
 T11B_RAT STANDARD: PRT; 401 AA.
 ID T11B_RAT
 AC 008727;
 DT 15-JUN-2002 (Rel. 41, Created)
 DT 15-JUN-2002 (Rel. 41, Last sequence update)
 DT 15-JUN-2002 (Rel. 41, Last annotation update)
 DE Tumor necrosis factor receptor superfamily member 11B precursor
 DE (osteoprotegerin).
 GN TNFRSF11B OR OPG.
 OS Rattus norvegicus (Rat).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
 OX NCBI_Taxid=10116;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE-Embryonic Intestine;
 RX MEDLINE-97262071; PubMed-9108485;
 RA Simonet M.S., Lacey D.L., Dunstan C.R., Kelley M., Chang M.-S.,
 RA Luthy R., Nguyen H.Q., Wooden S., Bennett L., Boone T., Shimamoto G.,

| | | | |
|----|--|----|--|
| RA | Derose M, Elliott R., Colombero A., Tan H.-L., Trail G., Sullivan J., | RA | Derose M, Elliott R., Colombero A., Tan H.-L., Trail G., Sullivan J., |
| RA | Davy E., Bucy N., Renshaw-Gegg L., Hughes T.M., Hill D., Pattison W., | RA | Davy E., Bucy N., Renshaw-Gegg L., Hughes T.M., Hill D., Pattison W., |
| RA | Campbell P., Sander S., Van G., Tarpley J., Derby P., Lee R., | RA | Campbell P., Sander S., Van G., Tarpley J., Derby P., Lee R., |
| RA | Snugs S., Boyle W.J., | RA | Snugs S., Boyle W.J., |
| RT | "Osteoprotegerin: a novel secreted protein involved in the regulation | RT | "Osteoprotegerin: a novel secreted protein involved in the regulation |
| RT | of bone density.". | RT | of bone density.". |
| RL | Cell 89:309-319.(1997). | RL | Cell 89:309-319.(1997). |
| CC | -1- FUNCTION: Acts as decoy receptor for RANKL and thereby neutralizes | CC | -1- FUNCTION: Acts as decoy receptor for RANKL and thereby neutralizes |
| CC | its function in osteoclastogenesis. Inhibits the activation of | CC | its function in osteoclastogenesis. Inhibits the activation of |
| CC | osteoclasts and promotes osteoclast apoptosis. Bone homeostasis | CC | osteoclasts and promotes osteoclast apoptosis. Bone homeostasis |
| CC | seems to depend on the local RANKL/OPG ratio. May also play a role | CC | seems to depend on the local RANKL/OPG ratio. May also play a role |
| CC | in preventing arterial calcification. May act as decoy receptor | CC | in preventing arterial calcification. May act as decoy receptor |
| CC | for TRAIL and protect against apoptosis. TRAIL binding blocks the | CC | for TRAIL and protect against apoptosis. TRAIL binding blocks the |
| CC | inhibition of osteoclastogenesis (By similarity). | CC | inhibition of osteoclastogenesis (By similarity). |
| CC | -1- SUBUNIT: Homodimer (By similarity). | CC | -1- SUBUNIT: Homodimer (By similarity). |
| CC | -1- SUBCELLULAR LOCATION: Secreted (By similarity). | CC | -1- SUBCELLULAR LOCATION: Secreted (By similarity). |
| CC | -1- INDUCTION: Upregulated by osteopontin. | CC | -1- INDUCTION: Upregulated by osteopontin. |
| CC | -1- SIMILARITY: CONTAINS 4 TNFR-CYS REPEATS. | CC | -1- SIMILARITY: CONTAINS 4 TNFR-CYS REPEATS. |
| CC | -1- SIMILARITY: CONTAINS 2 DEATH DOMAINS. | CC | -1- SIMILARITY: CONTAINS 2 DEATH DOMAINS. |
| CC | ----- | CC | ----- |
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| CC | or send an email to license@isb-sib.ch). | CC | or send an email to license@isb-sib.ch). |
| CC | ----- | CC | ----- |
| DR | EMBL: U94330; AAB53707.1; . | DR | EMBL: U94330; AAB53707.1; . |
| DR | HSSP: P25942; 1CDF. | DR | HSSP: P25942; 1CDF. |
| DR | InterPro: IPR000488; Death. | DR | InterPro: IPR000488; Death. |
| DR | InterPro: IPR001368; TNFR_C6. | DR | InterPro: IPR001368; TNFR_C6. |
| DR | Pfam: PF00020; TNFR_C6; 4. | DR | Pfam: PF00020; TNFR_C6; 4. |
| DR | ProDom: PD000771; TNFR_C6; 1. | DR | ProDom: PD000771; TNFR_C6; 1. |
| DR | SMART: SM00005; DEATH; 1. | DR | SMART: SM00005; DEATH; 1. |
| DR | SMART: SM00208; TNFR; 4. | DR | SMART: SM00208; TNFR; 4. |
| DR | PROSITE: PS50017; DEATH_DOMAIN; FALSE_NEG. | DR | PROSITE: PS50017; DEATH_DOMAIN; FALSE_NEG. |
| DR | PROSITE: PS00652; TNFR_NGFR_1; 1. | DR | PROSITE: PS00652; TNFR_NGFR_1; 1. |
| DR | PROSITE: PS50050; TNFR_NGFR_2; 2. | DR | PROSITE: PS50050; TNFR_NGFR_2; 2. |
| RW | Cytokine; Apoptosis; Glycoprotein; Repeat; Signal. | RW | Cytokine; Apoptosis; Glycoprotein; Repeat; Signal. |
| FT | CHAIN | FT | CHAIN |
| FT | 1 | FT | 1 |
| FT | 22 | FT | 22 |
| FT | 401 | FT | 401 |
| FT | 24 | FT | 24 |
| FT | 62 | FT | 62 |
| FT | 105 | FT | 105 |
| FT | 142 | FT | 142 |
| FT | 145 | FT | 145 |
| FT | 185 | FT | 185 |
| FT | 198 | FT | 198 |
| FT | 269 | FT | 269 |
| FT | 365 | FT | 365 |
| FT | 400 | FT | 400 |
| FT | 41 | FT | 41 |
| FT | 54 | FT | 54 |
| FT | 62 | FT | 62 |
| FT | 80 | FT | 80 |
| FT | 97 | FT | 97 |
| FT | 105 | FT | 105 |
| FT | 107 | FT | 107 |
| FT | 118 | FT | 118 |
| FT | 124 | FT | 124 |
| FT | 142 | FT | 142 |
| FT | 145 | FT | 145 |
| FT | 160 | FT | 160 |
| FT | 185 | FT | 185 |
| FT | 98 | FT | 98 |
| FT | 165 | FT | 165 |
| FT | 178 | FT | 178 |
| FT | 289 | FT | 289 |
| FT | 289 | FT | 289 |
| FT | 46192 MW; | FT | 46192 MW; |
| FT | FECC6A1F4DA573A CRC64; | FT | FECC6A1F4DA573A CRC64; |
| FT | SEQUENCE | FT | SEQUENCE |
| FT | 401 AA; | FT | 401 AA; |
| FT | 46192 MW; | FT | 46192 MW; |
| FT | FECC6A1F4DA573A CRC64; | FT | FECC6A1F4DA573A CRC64; |
| FT | SEQUENCE | FT | SEQUENCE |
| FT | 401 AA; | FT | 401 AA; |
| FT | 46192 MW; | FT | 46192 MW; |
| FT | FECC6A1F4DA573A CRC64; | FT | FECC6A1F4DA573A CRC64; |
| FT | SEQUENCE | FT | SEQUENCE |
| FT | 401 AA; | FT | 401 AA; |
| FT | 46192 MW; | FT | 46192 MW; |
| FT | FECC6A1F4DA573A CRC64; | FT | FECC6A1F4DA573A CRC64; |
| FT | SEQUENCE | FT | SEQUENCE |
| FT | 401 AA; | FT | |

| | | | | |
|-----------------------|-----------------|---------------|----------|------------|
| Query Match | 26.0% | Score 425.5 | DB 1 | Length 401 |
| Best Local Similarity | 39.58% | Pred. No. 4 | 6e-26 | |
| Matches 81 | Conservative 33 | Mismatches 86 | Indels 5 | Gaps 2 |

QY 34 PPTVPMRDLATGERLVCACCPGTFVQVRQCRDSDPTTCGCPRRHNYTQFWNLNLCRCRYCNV 93
Db 26 PKLHYDEPTGRQLCDCKCAPGYLLKQCTVRRKTLCPCCPDYSYSDSMHTSDCCVYSP 85

| | | | | | | | |
|----------|--|--|---|---------|--|--|--|
| Oy | | 94 | LCGRREEARACHTNTTHNACRCRPGFMAHAFCELEHNASCPGPAQVIAAPGPSQNTQCOPC | 153 | | | |
| Dd | | 86 | VCKELGYTKQKNCNTHNNVCCEBGRYLELEFCILKHNSCPGLGVLAGIPERTYVKRC | 145 | | | |
| Oy | | 154 | PPTGTSSASSSSSECCQPRNRCTAIGLAIVNGSSSHDTLCTSCGFPLSTRVGAEE--C | 211 | | | |
| Dd | | 146 | PDGFFSGCTSSAKAPCRKHTNCSLLGILOKGNATHDYN---CGSNEARDONCSDVTLC | 202 | | | |
| Oy | | 212 | ERAVIDPFAFDISIKRLQLRLAL | 236 | | | |
| Dd | | 203 | EBAFFRFAPVPKTIIPNLVLVSIDL | 227 | | | |
| RESULT 4 | | | | | | | |
| ID | T11B_MOUSE | STANDARD: | PRT: | 401 AA. | | | |
| AC | 008712; | 070202; | | | | | |
| DR | 15-JUN-2002 | (Rel. 41, | Created) | | | | |
| DT | 15-JUN-2002 | (Rel. 41, | Last sequence update) | | | | |
| DE | 15-JUN-2002 | (Rel. 41, | Last annotation update) | | | | |
| DE | Tumor necrosis factor receptor superfamily member 11b precursor (osteoprotegerin) (osteoclastogenesis inhibitory factor). | | | | | | |
| GN | TNFRSF11B OR OP OR OCIF. | | | | | | |
| OS | Mus musculus (Mouse). | | | | | | |
| OC | Eutheria; Metazoa; Chordata; Vertebrata; Euteleostomi; | | | | | | |
| CC | Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus. | | | | | | |
| OX | NCBI_TaxID=10090. | | | | | | |
| RN | [1] | | | | | | |
| RP | SEQUENCE FROM N.A. | | | | | | |
| RC | STRAIN=BALB/c; TISSUE=Kidney; | | | | | | |
| RX | MEDLINE=97262071; PubMed=9108485; | | | | | | |
| RA | Simone W.S., Lacey D.L., Dunstan C.R., Kelley M., Chang M.-S., | | | | | | |
| RA | Luethy R., Nguyen H.Q., Wooden S., Bennett L., Boone T., Shimamoto G., | | | | | | |
| RA | DeRose M., Elliott R., Colombero A., Tan H.-L., Trail G., Sullivan J., | | | | | | |
| RA | Davis E., Bucy N., Renshaw-Gegg L., Hughes T.M., Hill D., Pattison W., | | | | | | |
| RA | Campbell P., Sander S., Van G., Tarpley J., Derby P., Lee R., | | | | | | |
| RA | Suggs S., Boyle W.J.; | | | | | | |
| RT | Osteoprotegerin: a novel secreted protein involved in the regulation | | | | | | |
| RL | of bone density."; | | | | | | |
| RN | Cell 89:309-319(1997). | | | | | | |
| RN | [2] | | | | | | |
| RP | SEQUENCE FROM N.A., AND VARIANTS PRO-136; ARG-161; ASP-165; ALA-288 | | | | | | |
| RP | AND ARG-256. | | | | | | |
| RC | STRAIN=129/Ola, and NIH Swiss; TISSUE=Fibroblast; | | | | | | |
| RX | MEDLINE=968382527; PubMed=9714833; | | | | | | |
| RA | Mizuno A., Murakami A., Nakagawa N., Yasuda H., Tsuda E., Morinaga T., | | | | | | |
| RA | Higashino K.; | | | | | | |
| RT | Structure of the mouse osteoclastogenesis inhibitory factor (OCIF) | | | | | | |
| RT | gene and its expression in embryogenesis."; | | | | | | |
| RL | Gene 215:339-343(1998). | | | | | | |
| RN | [3] | | | | | | |
| RP | FUNCTION. | | | | | | |
| RX | MEDLINE=21060987; Pubmed=10952776; | | | | | | |
| RA | Min H., Morony S., Sarosi I., Dunstan C.R., Capparelli C., Scully S., | | | | | | |
| RA | Van G., Kaufman S., Kostenuik P.J., Lacey D.L., Boyle W.J., | | | | | | |
| RA | Simone W.S.; | | | | | | |
| RT | Osteoprotegerin reverses osteoporosis by inhibiting endosteal | | | | | | |
| RT | osteoclasts and prevents vascular calcification by blocking a process | | | | | | |
| RL | resembling osteoclastogenesis."; | | | | | | |
| RL | J. Exp. Med. | 192:463-474(2000). | | | | | |
| CC | -I- | FUNCTION: Acts as decoy receptor for RANKL and thereby neutralizes | | | | | |
| CC | | its function in osteoclastogenesis. Inhibits the activation of | | | | | |
| CC | | osteoclasts and promotes osteoclast apoptosis in vitro. Bone | | | | | |
| CC | | homeostasis seems to depend on the local RANKL/OPG ratio. May also | | | | | |
| CC | | play a role in preventing arterial calcification. May act as decoy | | | | | |
| CC | | receptor for TRAIL and protect against apoptosis. TRAIL binding | | | | | |
| CC | | blocks the inhibition of osteoclastogenesis. | | | | | |
| CC | -I- | SUBUNIT: Homodimer. | | | | | |
| CC | -I- | SUBCELLULAR LOCATION: Secreted. | | | | | |
| CC | -I- | TISSUE SPECIFICITY: Highly expressed in liver, lung, stomach, | | | | | |
| CC | | intestines and calvaria. Highly expressed in decidua and placenta, | | | | | |
| CC | | and in embryo. | | | | | |

CC -1- SUBCELLULAR LOCATION: Secreted.
CC -1- TISSUE SPECIFICITY: Highly expressed in liver, lung, stomach, intestines and calvaria. Highly expressed in decidua and placenta, and in embryo.
CC -1- DEVELOPMENTAL STAGE: Detected in embryo at high levels on day 7,

CC whereas expression decreases at day 11 and increases from day 15
 CC to 17. On day 15 found in developing bone primordia,
 CC brachiocephalic artery and ductus arteriosus, left main bronchus,
 CC abdominal aorta and midgut.
 CC -1- INDUCTION: Upregulated by TGF-beta and estrogens. Downregulated by
 CC 1,25-dihydroxyvitamin D3 and parathyroid hormone.
 CC -1- SIMILARITY: CONTAINS 4 TNFR-CYS REPEATS.
 CC -1- SIMILARITY: CONTAINS 2 DEATH DOMAINS.
 CC -----
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 CC -----
 DR EMBL: U94331; AAB53708.1; -
 DR EMBL: AB013898; BAA28269.1; -
 DR EMBL: AB013903; BAA33388.1; -
 DR EMBL: AB013899; BAA33388.1; JOINED.
 DR EMBL: AB013900; BAA33388.1; JOINED.
 DR EMBL: AB013901; BAA33388.1; JOINED.
 DR EMBL: AB013902; BAA33388.1; JOINED.
 DR HSSP: P25942; ICDF.
 DR MGD: MGI:109587; Tnf1sf11b.
 DR InterPro: IPR000488; Death.
 DR InterPro: IPR001368; TNFR_C6.
 DR Pfam: PF00020; TNFR_C6; 3.
 DR ProDom: PD000771; TNFR_C6; 1.
 DR SMART: SM00005; DEATH; 1.
 DR SMART: SM00208; TNFR; 4.
 DR PROSITE: PS50017; DEATH DOMAIN; 1.
 DR PROSITE: PS00652; TNFR_NGFR_1; 1.
 DR PROSITE: PS50050; TNFR_NGFR_2; 2.
 DR Receptor: Apoptosis; Glycoprotein; Repeat; Signal; Polymorphism.
 FT SIGNAL 1 21
 FT CHAIN 22 401
 FT REPEAT 24 62
 FT REPEAT 65 105
 FT REPEAT 107 142
 FT REPEAT 145 185
 FT DOMAIN 198 269
 FT SITE 283 365
 FT SITE 400 400
 FT DISULFID 41 54
 FT DISULFID 44 62
 FT DISULFID 65 80
 FT DISULFID 83 97
 FT DISULFID 107 118
 FT DISULFID 124 142
 FT DISULFID 145 160
 FT DISULFID 166 185
 FT CARBOHYD 98 98
 FT CARBOHYD 165 165
 FT CARBOHYD 178 178
 FT CARBOHYD 289 289
 FT VARIANT 138 138
 FT VARIANT 161 161
 FT VARIANT 165 165
 FT VARIANT 288 288
 FT VARIANT 296 296
 FT SEQUENCE 401 AA; 45923 MM; CAA6102D3B312470 CRC64;
 Query Match 26.0%; Score 424.5; DB 1; Length 401;
 Best Local Similarity 39.0%; Pred. No. 5.5e-26;

Matches 80; Conservative 32; Mismatches 88; Indels 5; Gaps 2;
 QY 34 PTYPWRAEGERGERLYACQCPGPFVQRCRDRSDPTGCPDRHYQTGFMYLERCRCNV 93
 DB 26 PKYLHYPERGHOLCKCAPGYLKHCHVRRKTLVPCPDHSTYSMTSHSDCYCSP 85
 QY 94 LCGREDEEACNATHNRACRCPRTGFPAHAGFCLEHASCPCGAGVIAPTSPONTQOCPC 153
 DB 86 VCKELQSVKQDCNTHNRVCEGEGRYLEIEFLCAKHSCPCGSGVAGTPERTYKCC 145
 QY 154 PGTFSASSSSSSQCPQHNCNTALGLALNPGSSHDLTCTGTFPLSTRVGAEE--C 211
 DB 146 PDGFFSGEFTSKAPCIKHTFNCSTFGLLIOGNATHDNV---CSGNREATQKCGIDVTLC 202
 QY 212 ERATVDPAFODISIKRLQRLDAL 236
 DB 203 EEAFFRAVPVKTIIPNWLVSALVDSL 227
 RESULT 5
 TRIB_HUMAN STANDARD; PRT; 461 AA.
 AC P20333; Q16042;
 DT 01-FEB-1991 (Rel. 17, Created)
 DT 15-JUN-2002 (Rel. 41, Last sequence update)
 DT 15-JUN-2002 (Rel. 41, Last annotation update)
 DE Tumor necrosis factor receptor superfamily member 1B precursor (Tumor
 DE necrosis factor receptor 2) (p80) (TNF-R2) (p5) (CD120) (Etanercept)
 DE [Contains: Tumor necrosis factor binding protein 2 (TNFIP1)].
 GN TNFRSF1B OR TNFR2 OR TNFR.
 OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
 OC NCBI_Taxid=9606;
 RN [1]
 RP MEDLINE-90260639; Pubmed-2160731;
 RA Smith C.A., Davis T., Anderson D., Solam L., Beckmann M.P., Jerzy R.,
 RA Dower S.K., Cosman D., Goodwin R.G.;
 RT "A receptor for tumor necrosis factor defines an unusual family of
 RT cellular and viral proteins";
 RL Science 248:1019-1023(1990).
 RN [2]
 RP MEDLINE-91045991; Pubmed-2172983;
 RA Kohno T., Brewer M.T., Baker S.L., Schwartz P.E., King M.W.,
 RA Hale K.K., Squires C.H., Thompson R.C., Vannice J.L.;
 RT "A second tumor necrosis factor receptor gene product can shed a
 RT naturally occurring tumor necrosis factor inhibitor";
 RL Proc. Natl. Acad. Sci. U.S.A. 87:8331-8335(1990).
 RN [3]
 RP MEDLINE-91045991; Pubmed-2172983;
 RA Kohno T., Brewer M.T., Baker S.L., Schwartz P.E., King M.W.,
 RA Hale K.K., Squires C.H., Thompson R.C., Vannice J.L.;
 RT "A second tumor necrosis factor receptor gene product can shed a
 RT naturally occurring tumor necrosis factor inhibitor";
 RL Proc. Natl. Acad. Sci. U.S.A. 87:8331-8335(1990).
 RN [4]
 RP MEDLINE-96299745; Pubmed-8661109;
 RA Beltinger C.P., White P.S., Maris J.M., Sulman E.P., Jensen S.J.,
 RA Lepassier D., Stallard B.J., Goeddel D.V., Desauvage F.J.,
 RA Brodeur G.M.;
 RT "Physical mapping and genomic structure of the human TNFR2 gene";
 RL Genomics 35:94-100(1996).
 RN [5]
 RP MEDLINE-91370690; Pubmed-1966549;
 RA Dembic Z., Loetscher H., Gubler U., Pan Y.C., Lahn H.W., Gentz R.,
 RA Brockhaus M., Lesslauer W.;
 RT "Two human TNF receptors have similar extracellular, but distinct
 RT intracellular, domain sequences";
 RL Cytokine 2:231-237(1990).
 RN [6]
 RP MEDLINE-90349572; Pubmed-2166946;
 RA Heller R.A., Song K., Onasch M.A., Fischer W.H., Chang D.,
 RA Ringold G.M.;
 RT "Complementary DNA cloning of a receptor for tumor necrosis factor
 RT and demonstration of a shed form of the receptor";

RL Proc. Natl. Acad. Sci. U.S.A. 87:6151-6155(1990).
 RN [6]
 RX SEQUENCE OF 27-31.
 RP MEDLINE-90110215; PubMed-2153136;
 RA Engelmann H., Novick D., Wallach D.;
 RT "Two tumor necrosis factor-binding proteins purified from human
 RT urine. Evidence for immunological cross-reactivity with cell surface
 RT tumor necrosis factor receptors";
 RL J. Biol. Chem. 265:1531-1536(1990).
 RN [7]
 RX SEQUENCE OF 23-40; 65-69; 136-141; 300-306 AND 346-362.
 RP MEDLINE-91056048; PubMed-2173696;
 RA Loetscher H., Schlaeeger E.J., Lahn H.-W., Pan Y.-C.E., Lesslauer W.,
 RA Brockhaus M.;
 RT "Purification and partial amino acid sequence analysis of two
 RT distinct tumor necrosis factor receptors from HL60 cells.";
 RL J. Biol. Chem. 265:20131-20138(1990).
 RN [8]
 RP CHARACTERIZATION
 RX MEDLINE-93016040; PubMed-1328224;
 RA Pennica D., Lam V.T., Mize N.K., Weber R.F., Lewis M., Fendly B.M.,
 RA Lipari M.T., Goeddel D.V.;
 RT "Biochemical properties of the 75-kDa tumor necrosis factor receptor.
 RT Characterization of ligand binding, internalization, and receptor
 RT phosphorylation.";
 RL J. Biol. Chem. 267:21172-21178(1992).
 RN [9]
 RP X-RAY CRYSTALLOGRAPHY (2.3 ANGSTROMS) OF 419-428 IN COMPLEX WITH
 RP TRAF2.
 RX MEDLINE-99221490; PubMed-10206649;
 RA Park Y.C., Burditt V., Villa A.R., Tong L., Wu H.;
 RT "Structural basis for self-association and receptor recognition of
 RT human TRAF2";
 RL Nature 398:533-538(1999).
 CC -1- FUNCTION: Receptor with high affinity for TNFSF2/TNF-alpha and
 CC approximately 5-fold lower affinity for homotrimeric
 CC TNFSF1/lymphotoxin-alpha.
 CC -1- SUBCELLULAR LOCATION: Type I membrane protein and secreted.
 CC -1- PTM: Phosphorylated; mainly on serine residues and with a very low
 CC level on threonine residues.
 CC -1- PTM: A soluble form (tumor necrosis factor binding protein 2) is
 CC produced from the membrane form by proteolytic processing.
 CC -1- PHARMACEUTICAL: Available under the name Embrel (Immunex and
 CC Wyeth-Ayerst). Used to treat moderate to severe rheumatoid
 CC arthritis (RA). Embrel consist of the extracellular ligand-binding
 CC portion of TNFR2 linked to an Immunoglobulin Fc chain. It binds to
 CC TNF-alpha and blocks its interactions with receptors.
 CC -1- SIMILARITY: COMPAINS 4 TNFR-CYS REPEATS.
 CC -1- DATABASE: NAME=PRO; NOTE=CD guide CD120b entry;
 CC WWW="http://www.ncbi.nlm.nih.gov/prov/cd/cd120b.htm";
 CC -1- DATABASE: NAME=Embrel; NLM=clinical information on Embrel;
 CC WWW="http://www.embrelinfo.com/".
 CC -----
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 CC or send an email to license@isb-sib.ch).
 CC -----
 DR EMBL: M32315; AAC59929.1; -;
 DR EMBL: U52165; AAC50622.1; -;
 DR EMBL: U52156; AAC50622.1; JOINED.
 DR EMBL: U52157; AAC50622.1; JOINED.
 DR EMBL: U52158; AAC50622.1; JOINED.
 DR EMBL: U52159; AAC50622.1; JOINED.
 DR EMBL: U52160; AAC50622.1; JOINED.
 DR EMBL: U52161; AAC50622.1; JOINED.
 DR EMBL: U52162; AAC50622.1; JOINED.
 DR EMBL: U52163; AAC50622.1; JOINED.
 DR EMBL: U52164; AAC50622.1; JOINED.
 DR EMBL: M55994; AAA36755.1; -;

| | |
|-------------|---|
| DR | EMBL; S63368; AAB19824.2; - |
| DR | EMBL; M35857; AAA63262.1; -. |
| DR | PIR; A35356; A35356. |
| DR | PIR; A36007; A36007. |
| DR | PIR; A36475; A36475. |
| DR | PIR; B35010; B35010. |
| DR | PIR; A23666; A23666. |
| DR | PDB; 1CA9; 12-APR-99. |
| DR | Genew; HGNC:11917; TNFRSF1B. |
| DR | MIM; 191191; -. |
| DR | InterPro; IPRO01368; TNFR_c6. |
| DR | Pfam; PF00020; TNFR_c6; 4. |
| DR | ProDom; PD000771; TNFR_c6; 1. |
| DR | SMART; SM00208; TNFR; 4. |
| DR | PROSITE; PS00652; TNFR_NGFR_1; 2. |
| DR | PROSITE; PS50050; TNFR_NGFR_2; 4. |
| KW | Receptor; Transmembrane; Glycoprotein; Repeat; Signal; |
| KW | Phosphorylation; Pharmaceutical; 3D-structure. |
| FT | SIGNAL |
| FT | CHAIN |
| FT | FT |
| FT | CHAIN |
| FT | CHAIN |
| FT | CHAIN |
| FT | DOMAIN |
| FT | TRANSMEM |
| FT | DOMAIN |
| FT | REPEAT |
| FT | REPEAT |
| FT | REPEAT |
| FT | REPEAT |
| FT | DISULFID |
| FT | DISULFID |
| FT | DISULFID |
| FT | DISULFID |
| FT | DISULFID |
| FT | DISULFID |
| FT | DISULFID |
| FT | DISULFID |
| FT | CARBOHYD |
| FT | CARBOHYD |
| FT | CONFLICT |
| FT | CONFLICT |
| FT | CONFLICT |
| FT | CONFLICT |
| FT | CONFLICT |
| SO | SEQUENCE |
| Query Match | Best Local Similarity |
| Matches | Conservative |
| 96; | Score 351.5; DB 1; Length 461; |
| 21.5%; | Pred. No. 2; 9e-20; |
| 29.8%; | Mismatches 122; Indels 61; Gaps 12 |
| 43; | |
| QY | 8 GLSLCLLVLPALPLPVPVAVRGVAETPRYPMDATGE-----RLVCAOCPG 55 |
| Db | 13 GLELMAAHLRA-----QVATFPAP-----EPGSTCLKREYDQTAMCCSKSPG 60 |
| QY | 56 TVQVRRCRDSPPTGPCPPRHYYTFMWNLERCRCYNVLAGEBEERARACHATHNRACR 115 |
| Db | 61 QHAKVCFTKSTPDVDCSDSTYTQLMMWPBCISCGSRCSDDVETQACTREQNRICTC 120 |
| QY | 116 RTGFEPFAHG-----PCLEHASCPGAGVIAPGTFSQNTQCPCPGTFFSASSSSSQOC 169 |
| Db | 121 RPQWICALSKOEGRCLCAPLRKCRRGFGFARGRETSPVCKPCAPGTFSMTSTDICR 180 |
| QY | 170 PHNHCALGLIALNVPESSHDFLCSCGPFLLSTPVGAECCEBAVIDFAFDISTIKRL 229 |
| Db | 181 PHTICNVYA-----ITRNMSMDVACTSTS--PTRSAIPGANILPOV-----STNSQHT 227 |
| QY | 230 QRLQLALEAPE-----GMGPTRRA-----GRAALDKLRLRTTELIGAQDALIVRLLOAL 280 |
| Db | 228 QRPREESTAPRSIFLLPMGPSRPAGSGTDPAFLPGLIVGYTAL-----GLLTIGVNCY 282 |
| QY | 281 ---RVARNP-GLESVVEREFLP 298 |
| Db | 283 IMTVQKKRKPLCGLOREAKVDNP 304 |

RESULT 6

| TRIM_MOUSE | STANDARD | PRT | 474 AA |
|---|----------|-----|--------|
| AC P25119; P97893; | | | |
| DT 01-MAY-1992 (Rel. 22, Created) | | | |
| DT 01-MAY-1992 (Rel. 22, Last sequence update) | | | |
| DT 15-JUN-2002 (Rel. 41, Last annotation update) | | | |
| DE Tumor necrosis factor receptor superfamily member 1B precursor (Tumor necrosis factor receptor 2) (TNF-R2) (P/5). | | | |
| DE TNFRSF1B OR TNFR2 OR TNFR-2. | | | |
| OS Mus musculus (Mouse). | | | |
| OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus. | | | |
| OX NCBI_TaxID=10090; | | | |
| RP SEQUENCE FROM N.A. | | | |
| RX MEDLINE=9187885; PubMed=1849278; | | | |
| RA Lewis M., Tartaglia L.A., Lee A., Bennett G.L., Rice G.C., | | | |
| RA Wong G.H., Chen E.Y., Goeddel D.V.; | | | |
| RT "Cloning and expression of cDNAs for two distinct murine tumor necrosis factor receptors demonstrate one receptor is species specific." | | | |
| RT Proc. Natl. Acad. Sci. U.S.A. 88:2830-2834(1991). | | | |
| RN [2] | | | |
| RP SEQUENCE FROM N.A. | | | |
| RX MEDLINE=91246168; PubMed=1645445; | | | |
| RA Goodwin R.G., Anderson D., Jerzy R., Davis T., Brannan C.I., | | | |
| RA Copeland N.G., Jenkins N.A., Smith C.A.; | | | |
| RT "Molecular cloning and expression of the type 1 and type 2 murine RT receptors for tumor necrosis factor." | | | |
| RT Mol. Cell. Biol. 11:3020-3026(1991). | | | |
| RN [3] | | | |
| RP SEQUENCE OF 1-26 FROM N.A. | | | |
| RC STRAIN=NOD; | | | |
| RA Jacob C.O., Liu J.; | | | |
| RL Submitted (JAN-1996) to the EMBL/GenBank/DBJ databases. | | | |
| RN [4] | | | |
| RP TISSUE=Liver; | | | |
| RA Kissomieris M., Fellows R., Feldmann M., Chernajovsky Y.; | | | |
| RL Submitted (MAY-1995) to the EMBL/GenBank/DBJ databases. | | | |
| CC -1- FUNCTION: Receptor with high affinity for TNFSF2/TNF-alpha and approximately 5-fold lower affinity for homotrimeric TNFSF1/Lymphotoxin-alpha (by similarity). | | | |
| CC -1- SUBCELLULAR LOCATION: Type I membrane protein. | | | |
| CC -1- SIMILARITY: CONTAINS 4 TNFR-CYS REPEATS. | | | |
| CC | | | |
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| CC ----- | | | |
| DR EMBL: M60469; AAA39752.1; - | | | |
| DR EMBL: M59378; AAA40463.1; - | | | |
| DR EMBL: U39488; AAA85021.1; - | | | |
| DR EMBL: X87128; CAA60618.1; - | | | |
| DR PIR: B38634; B38634. | | | |
| DR HSSP: P19438; IMCF. | | | |
| DR MGD: MGI:1314883; Tnfisf1b. | | | |
| DR InterPro: IPR001368; TNFR_C6. | | | |
| DR Pfam: PF00020; TNFR_C6; 4. | | | |
| DR ProDom: PD000771; TNFR_C6; 1. | | | |
| DR SMART: SM00208; TNFR; 4. | | | |
| DR PROSITE: PS00652; TNFR_NGFR_1; 2. | | | |
| DR PROSITE: PS50050; TNFR_NGFR_2; 3. | | | |
| KW Receptor; Transmembrane; Glycoprotein; Repeat; Signal. | | | |
| FT SIGNAL 1 22 | | | |
| FT CHAIN 23 474 | | | |
| RP TUMOR NECROSIS FACTOR RECEPTOR | | | |

RESULT 7

| TNR3_HUMAN | STANDARD | PRT | 435 AA |
|---|----------|-----|--------|
| AC P36941; | | | |
| DT 01-JUN-1994 (Rel. 29, Created) | | | |
| DT 01-JUN-1994 (Rel. 29, Last sequence update) | | | |
| DT 15-JUN-2002 (Rel. 41, Last annotation update) | | | |
| DE Tumor necrosis factor receptor superfamily member 3 precursor (Lymphotoxin-beta receptor) (Tumor necrosis factor receptor 2 related protein) (Tumor necrosis factor C receptor). | | | |
| DE LTR OR TNFRSF3 OR TNFR. | | | |
| OS Homo sapiens (Human). | | | |
| OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Homiidae; Homo. | | | |
| OX NCBI_TaxID=9606; | | | |
| RP SEQUENCE FROM N.A. | | | |
| RX MEDLINE=93252381; PubMed=8486360; | | | |
| RA Baens M., Chaffanet M., Cassiman J.J., den Berghe H., Marynen P.; | | | |
| RT "Construction and evaluation of a hncDNA library of human 12p transcribed sequences derived from a somatic cell hybrid." | | | |
| RT Genomics 16:214-218(1993). | | | |
| RN [2] | | | |
| RP SEQUENCE FROM N.A. | | | |
| RC TISSUE=Lung; | | | |

Query Match 20.3%; Score 332.5; DB 1; Length 474;
Best Local Similarity 29.7%; Pred. No. 8.9e-19;
Matches 81; Conservative 44; Mismatches 109; Indels 39; Gaps 9;

| FT | DOMAIN | 23 | 258 | SUPERFAMILY MEMBER 1B. |
|-------------|---------|-----------|-------------------------|-------------------------------------|
| FT TRANSMEM | 259 | 288 | | EXTRACELLULAR (POTENTIAL). |
| FT DOMAIN | 289 | 474 | | CYTOPLASMIC (POTENTIAL). |
| FT REPEAT | 39 | 77 | | TNFR-CYS 1. |
| FT REPEAT | 78 | 119 | | TNFR-CYS 2. |
| FT REPEAT | 120 | 164 | | TNFR-CYS 3. |
| FT REPEAT | 165 | 203 | | TNFR-CYS 4. |
| FT DISULFID | 40 | 54 | | BY SIMILARITY. |
| FT DISULFID | 55 | 68 | | BY SIMILARITY. |
| FT DISULFID | 58 | 76 | | BY SIMILARITY. |
| FT DISULFID | 79 | 94 | | BY SIMILARITY. |
| FT DISULFID | 97 | 111 | | BY SIMILARITY. |
| FT DISULFID | 101 | 119 | | BY SIMILARITY. |
| FT DISULFID | 121 | 127 | | BY SIMILARITY. |
| FT DISULFID | 136 | 145 | | BY SIMILARITY. |
| FT DISULFID | 139 | 163 | | BY SIMILARITY. |
| FT CARBOHYD | 69 | 69 | | BY SIMILARITY. |
| FT CARBOHYD | 195 | 195 | | N-LINKED (GLCNAC. . .) (POTENTIAL). |
| FT CARBOHYD | 195 | 195 | | N-LINKED (GLCNAC. . .) (POTENTIAL). |
| SO SEQUENCE | 474 AA; | 50319 MM; | 462EAE398C4D5653 CRC64; | |

Query Match 20.3%; Score 332.5; DB 1; Length 474;
Best Local Similarity 29.7%; Pred. No. 8.9e-19;
Matches 81; Conservative 44; Mismatches 109; Indels 39; Gaps 9;

| QY | 46 | RIVACQCPGTFVQPCRRDSDPTGCGPCPPPHYQFMNLYERCRVCNVLCGEREERAC | 105 |
|----|-----|---|-----|
| DB | 52 | QMCACKCPGGYVHFNCNKTSDIVCADCEASMYQVNWQFETCSCSSCTDDVEIRAC | 111 |
| QY | 106 | HATNRCRCRTGFE---AHAGF---CLEHASCPPGAGVIAPTPSONTQCCPCPGTF | 158 |
| DB | 112 | TKQNRVYACACAGKATKTHSSGRCQMRKSGPFGVASSAPNGNVLCACAGTF | 171 |
| QY | 159 | SASSSSSQCPHRCNCTALGIALNVPGSSSHDTCT---SCGFPILSTRVGAEECERA | 214 |
| DB | 172 | SDTTSYDVCPRPHICSIILA---IPGNASTDAVCADESPILSAIPRTLYVSOPEPTRSQ | 227 |
| QY | 215 | VIDFVARQDISIKRLQQLQALAEPEGMPRP---RAGAAQLKLRRLFTLLAQD | 269 |
| DB | 228 | PLD---QEPGSPSILVSL---GSTPIIEQSTKGISLIGLVISL----- | 272 |
| QY | 270 | GALLVRLQAL---RYARMPLGRSVRERLP | 298 |
| DB | 273 | GLMLGLVNCIIIVQRKKKPCCLORDAKVHPV | 305 |

RA Strausberg R.;
 RL Submitted (APR-2002) to the EMBL/GenBank/DBJ databases.
 RN [3]
 RP FUNCTION
 RA MEDLINE-94225209; PubMed-8171323;
 RA Crowe P.D., van Arsden T.L., Walter B.N., Ware C.F., Hession C.,
 RA Ehrenfeld B., Browning J.L., Din W.S., Goodwin R.G., Smith C.A.;
 RT "A lymphotoxin-beta-specific receptor.";
 RL Science 264:707-710(1994).
 RN [4]
 RP CHARACTERIZATION
 RA MEDLINE-99223511; PubMed-10207006;
 RA Wu M.-Y., Wang P.-Y., Han S.-H., Hsieh S.-L.;
 RT "The cytoplasmic domain of the lymphotoxin-beta receptor mediates cell
 death in HeLa cells.";
 RL J. Biol. Chem. 274:11868-11873(1999).
 RN [5]
 RP FUNCTION
 RA MEDLINE-20261554; PubMed-10799510;
 RA Rooney I.A., Butrovich K.D., Glass A.A., Borboroglu S., Benedict C.A.,
 RA Whitbeck J.C., Cohen G.H., Eisenberg R.J., Ware C.F.;
 RT "The lymphotoxin-beta receptor is necessary and sufficient for
 LIGHT-mediated apoptosis of tumor cells.";
 RL J. Biol. Chem. 275:14307-14315(2000).
 CC - FUNCTION: Receptor for the heterotrimeric lymphotoxin containing
 CC LTA and LTB, and for TNFS14/LIGHT. Promotes apoptosis via TRAF3
 CC and TRAF5. May play a role in the development of lymphoid organs.
 CC - SUBUNIT: Self-associates.
 CC - SUBCELLULAR LOCATION: Type I membrane protein.
 CC - SIMILARITY: CONTAINS 4 TNFR-CYS REPEATS.
 CC -----
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 CC -----
 DR EMBL: L04270; AAA36757.1; -
 DR EMBL: BC026262; AAA26262.1; -
 DR HSSP: P25942; ICDF.
 DR Genew: HGNC:6718; LTBR.
 DR MIM: 600979; -
 DR InterPro: IPR001368; TNFR_c6.
 DR Pfam: PF00020; TNFR_c6; 4.
 DR Prodom: PD000771; TNFR_c6; 1.
 DR SMART: SM00208; TNFR_4.
 DR PROSITE: PS00652; TNFR_NGFR_1; 2.
 DR PROSITE: PS00500; TNFR_NGFR_2; 3.
 KW Receptor; Apoptosis; Transmembrane; Glycoprotein; Repeat; Signal.
 FT SIGNAL 1 30
 FT CHAIN 31 435
 FT DOMAIN 31 227
 FT TRANSMEM 228 248
 FT DOMAIN 249 435
 FT REPEAT 249 435
 FT REPEAT 42 81
 FT REPEAT 82 124
 FT REPEAT 125 168
 FT REPEAT 169 211
 FT DISULFID 43 58
 FT DISULFID 59 72
 FT DISULFID 62 80
 FT DISULFID 83 98
 FT DISULFID 101 116
 FT DISULFID 104 124
 FT DISULFID 126 132
 FT DISULFID 139 148
 FT DISULFID 142 167
 FT DISULFID 170 185
 FT CARBOHYD 40 40
 FT CARBOHYD 177 177

SO SEQUENCE 435 AA; 46709 MW; 62462656022F656F CRC64;
 Query Match 19.3%; Score 315; DB 1; Length 435;
 Best Local Similarity 31.8%; Pred. No. 1,8e-17;
 Matches 89; Conservative 29; Mismatches 120; Indels 42; Gaps 12;
 QY 3 ALEGPGLSLCLVLPALLPVPVAVGAVERPTY-----PWMDA-----ETGERLVCAQC 52
 DB 6 ATSAPGLAWGPIVLGFLGLAASQPAV---PPVASENQTCDQKEVEYEPHRIICSRG 62
 QY 53 PGRTFYQRCRDRSDPTGCPCPRHNYTPWNL-----ERCYCNVLCGEFEERARCNHTH 109
 DB 63 PGRTYVSANCSRIKRTVCAICENSYENHWNLTICQLCRPDPAWG--LEEIAPCTSR 120
 QY 110 NRCRCRTGFFAHAGCLE--H-----ASCPGA-GVIAPGTPSONTCQCPGTFSSAS 162
 DB 121 KTCRCQCPMFC-AMALECTHCELLSDCPGTEALNDEVKGNHHCYPCAGHFPQTS 179
 QY 163 SSSEOCQPHRNCTALGLALNVPSSSHDTLCTGCFPLSTRVPAEBCERAVIDFAFQ 222
 DB 180 SPARQCPHTRCENGLVPAAGTQSDTYCKNPLE-PLPPMSGTLMILAVLPLAFEL 238
 QY 223 DIS-----IKRLQRLQALEPBGMGPPRAG 249
 DB 239 LATVFSCTKSHPSICRLGSLK--RRQGEQPPVAG 276
 RESULT 8
 TR21_MOUSE
 ID TR21_MOUSE STANDARD; PRT; 655 AA.
 AC Q9EPD5; Q91KH9; Q91W77;
 DT 15-JUN-2002 (Rel. 41, Created)
 DR 15-JUN-2002 (Rel. 41, Last sequence update)
 DE 15-JUN-2002 (Rel. 41, Last annotation update)
 DE Tumor necrosis factor receptor superfamily member 21 precursor (TNFR-
 DE related death receptor-6) (Death receptor 6).
 GN TNFRSF21 OR DR6.
 OS Mus musculus (Mouse).
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
 OX NCBI_TaxID=10090;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC STRAIN=C57BL/6; TISSUE=Kidney;
 RA Isogai D., Ichino M., Yoshinari M., Yamaura A., Kurokawa F.,
 RA Minami M.;
 RT "Mouse DR6: mouse homolog of human TNFR-related death receptor-6
 RT (DR6).";
 RL Submitted (NOV-2000) to the EMBL/GenBank/DBJ databases.
 RN [2]
 RP SEQUENCE FROM N.A.
 RC STRAIN=BALB/c; TISSUE=Kidney;
 RA Kim V., Machleidt T., Shi W.-X., Wang X., Cai Z.;
 RT "Murine DR6: murine TNFR-related death receptor-6.";
 RL Submitted (JUL-2001) to the EMBL/GenBank/DBJ databases.
 RN [3]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Kidney;
 RA Strausberg R.;
 RL Submitted (OCT-2001) to the EMBL/GenBank/DBJ databases.
 RN [4]
 RP FUNCTION
 RA MEDLINE-21571606; PubMed-11714751;
 RA Zhao H., Yan M., Wang H., Erickson S., Grewal I.S., Dixit V.M.;
 RT "Impaired c-Jun amino terminal kinase activity and T cell
 RT differentiation in death receptor 6-deficient mice.";
 RL J. Exp. Med. 194:1441-1448(2001).
 CC - FUNCTION: May activate NF-kappa-B and promote apoptosis (By
 CC similarity). May activate JNK and be involved in T-cell
 CC differentiation.
 CC - FUNCTION: May activate NF-kappa-B and JNK and promote apoptosis.
 CC May be involved in T-cell differentiation.
 CC - SUBCELLULAR LOCATION: Type I membrane protein (Probable).
 CC -----


```

OY 69 TCGPCPPRHYYTFMNYLERCRVCNVLGGEREERARACHATNRACRGTGF-----AH 122
DB 64 OCTPGSGGTFTSRNNHLPACLSGCRNSNOVETRSCTNTHNRICECSGYCILLKSSG 123
OY 123 AGFCLHASCPCPGAGVIAPGTPSONTOCPCPGTFSASSSSSECCOPHRNCTALGLAN 182
DB 124 CKACVSQTKCGIGYGV-SGHTSVGDVICSFCGFGYSHTVSSADCEPVPNTFNYIDE 182
OY 183 VPGSSSHDTLCTSCGTGFPPLSTRVPGAE 209
DB 183 ILLYVNDPSTCRRTTTTGISESILTSE 209

RESULT 12
CRMB_CAMPS STANDARD: PRT: 349 AA.
AC Q8UYA7;
DT 15-JUN-2002 (rel. 41, Last sequence update)
DT 15-JUN-2002 (rel. 41, Last annotation update)
DE Soluble TNF receptor II precursor (cytokine response modifying protein
B).
GN (CRMB1 OR CMP2L OR CMLV002) AND (CRMB2 OR CMP205R OR CMLV210).
OS Camelpox virus (strain CMS), and
OC Camelpox virus (strain M-96).
OC Viruses; dsDNA viruses, no RNA stage; Poxviridae; Chordopoxvirinae;
OC Orthopoxvirus.
OX NCBI_TaxID=203172, 203173;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=CMS;
RX PubMed=11907336;
RA Gubser C., Smith G.L.;
RT "The sequence of camelpox virus shows it is most closely related to
RT variola virus, the cause of smallpox.";
RT J. Gen. Virol. 83:855-872(2002).
RN [2]
RP SEQUENCE FROM N.A.
RC STRAIN=M-96;
RA Alfonso C.L., Tulman E.R., Lu Z., Zsak L., Zaitsev V.L.,
RA Kandybekova U.Z., Sandybaev N.T., Kutish G.F., Rock D.L.;
RT "The genome of camelpox virus.";
RT Submitted (OCT-2001) to the EMBL/Genbank/DBD databases.
RL -1- FUNCTION: Receptor for TNF-alpha and TNF-beta. May contribute to
CC the modification of TNF-mediated antiviral processes (By
CC similarity).
CC -1- SUBCELLULAR LOCATION: Secreted (By similarity).
CC -1- SIMILARITY: CONTAINS 2 TNFR-CYS REPEATS.
CC -----
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CC or send an email to license@isb-sib.ch).
CC -----
DR EMBL: AY009089; AAG37456.1; -
DR EMBL: AY009089; AAG37118.1; -
DR EMBL: AF438165; AAL73920.1; -
DR EMBL: AF438165; AAL73917.1; -
DR InterPro: IPR001368; TNFR_C6.
DR Pfam: PF00020; TNFR_C6; 2.
DR SMART; SM00208; TNFR_3.
DR PROSITE; PS00652; TNFR_NGFR_1; 2.
DR PROSITE; PS50050; TNFR_NGFR_2; 2.
KW Receptor; Glycoprotein; Repeat; Signal.
FT SIGNAL 1 19
FT CHAIN 20 349 SOLUBLE TNF RECEPTOR II.
FT REPEAT 31 65 TNFR-CYS 1.
FT REPEAT 67 108 TNFR-CYS 2.
FT DISULFID 32 43 BY SIMILARITY.
FT DISULFID 44 57 BY SIMILARITY.

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FT DISULFID 47 65 BY SIMILARITY.
FT DISULFID 68 83 BY SIMILARITY.
FT DISULFID 86 100 BY SIMILARITY.
FT DISULFID 90 108 BY SIMILARITY.
FT CARBOHYD 101 101 N-LINKED (GLCNAC. . .) (POTENTIAL).
FT CARBOHYD 189 189 N-LINKED (GLCNAC. . .) (POTENTIAL).
FT CARBOHYD 248 248 N-LINKED (GLCNAC. . .) (POTENTIAL).
SQ SEQUENCE 349 AA; 38064 MW; EA412AF91E087F3 CRC64;

Query Match 16.0%; Score 261.5; DB 1; Length 349;
Best local similarity 29.0%; Pred. No. 2,1e-13;
Matches 60; Conservative 33; Mismatches 101; Indels 13; Gaps 3;

OY 9 ISLLCLVIALPALLPVPAVGVAEPTTYFWRDAETGERLVCACQCPGTFVQPCRRDSPT 68
DB 10 LFLSCIIINGRDVTPYAPNSGKCKDNEY-----KRHNLCCLSCPPTGYASRLCDSKTYT 63
OY 69 TCGPCPPRHYYTFMNYLERCRVCNVLGGEREERARACHATNRACRGTGF-----AH 122
DB 64 OCTPGSGGTFTSRNNHLPACLSGCRNSNOVETRSCTNTHNRICECSGYCILLKSSG 123
OY 123 AGFCLHASCPCPGAGVIAPGTPSONTOCPCPGTFSASSSSSECCOPHRNCTALGLAN 182
DB 124 CKACVSQTKCGIGYGV-SGHTSAGDVICSFCGLGYSRTVSSADCEPVPNTFNYIDE 182
OY 183 VPGSSSHDTLCTSCGTGFPPLSTRVPGAE 209
DB 183 ILLYVNDPSTCRRTTTTGISESISTSE 209

RESULT 13
CRMB_COMPX STANDARD: PRT: 351 AA.
AC Q73559;
DT 15-JUN-2002 (rel. 41, Created)
DT 15-JUN-2002 (rel. 41, Last sequence update)
DT 15-JUN-2002 (rel. 41, Last annotation update)
DE Soluble TNF receptor II precursor (cytokine response modifying protein
B).
GN (CRMB1 OR D2L) AND (CRMB2 OR H4R).
OS Complex virus (CPV).
OC Viruses; dsDNA viruses, no RNA stage; Poxviridae; Chordopoxvirinae;
OC Orthopoxvirus.
OX NCBI_TaxID=10243;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=GRI-90 / Grishak;
RX MEDLINE=98229462; PubMed=9568042;
RA Shechelkunov S.N., Saitonov P.F., Totmenin A.V., Petrov N.A.,
RA Ryazankina O.I., Guttorov V.V., Kotwal G.J.;
RT "The genomic sequence analysis of the left and right species-specific
RT terminal region of a complex virus strain reveals unique sequences and
RT a cluster of intact ORFs for immunomodulatory and host range
RT proteins.";
RT Virology 243:432-460(1998).
RN [2]
RP FUNCTION.
RC STRAIN=Brighton red;
RX PubMed=8091665;
RA Hu F.Q., Smith C.A., Pickup D.J.;
RT "Complex virus contains two copies of an early gene encoding a soluble
RT secreted form of the type II TNF receptor.";
RL Virology 204:343-356(1994).
CC -1- FUNCTION: Receptor for TNF-alpha and TNF-beta. May contribute to
CC the modification of TNF-mediated antiviral processes.
CC -1- SUBCELLULAR LOCATION: Secreted.
CC -1- SIMILARITY: CONTAINS 2 TNFR-CYS REPEATS.
CC -----
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CC -----

DR EMBL: Y11842; CAA72578.1; -

DR EMBL: Y15035; CAA75306.1; -

DR HSP: O14763; IDOG.

DR InterPro: IPR001368; TNFR_c6.

DR Pfam: PF00020; TNFR_c6; 2.

DR SMART: SM00208; TNFR; 2.

DR PROSITE: PS00652; TNFR_NGFR_1; 2.

DR PROSITE: PS50050; TNFR_NGFR_2; 2.

KW Receptor: Glycoprotein; Repeat; Signal.

FT SIGNAL 1 19 POTENTIAL.

FT CHAIN 20 351 SOLUBLE TNF RECEPTOR II.

FT REPEAT 31 67 TNFR-CYS 1.

FT REPEAT 69 110 TNFR-CYS 2.

FT DISULFID 32 43 BY SIMILARITY.

FT DISULFID 44 57 BY SIMILARITY.

FT DISULFID 47 67 BY SIMILARITY.

FT DISULFID 70 85 BY SIMILARITY.

FT DISULFID 88 102 BY SIMILARITY.

FT DISULFID 92 110 BY SIMILARITY.

FT CARBOHYD 103 103 N-LINKED (GLCNAC. . .) (POTENTIAL).

FT CARBOHYD 191 191 N-LINKED (GLCNAC. . .) (POTENTIAL).

FT CARBOHYD 250 250 N-LINKED (GLCNAC. . .) (POTENTIAL).

SO SEQUENCE 351 AA; 38253 MW; 57CAE73BE45ED7C7 CRC64;

Query Match 15.88; Score 258.5; DB 1; Length 351;

Best Local Similarity 29.28; Pred. No. 3.6e-13;

Matches 61; Conservative 34; Mismatches 99; Indels 15; Gaps 4;

QY 9 LSLICLVLPALPLPVAVGVAETPTYPMDAETGRIVCAOCPPTFVQRC--RRDS 66

DB 10 LFTSCITINGNDIAPHAAPNSKCKDNEY-----NRHNLCCSPGPGTVASRLCDSKTNT 63

QY 67 PTTGCPPPRHYYQFMNLECRRCYNYLGEREEBARACHATNRRACRRTGFF----- 120

DB 64 NTGCTPGSGFTFSRRNHLPACLSGCRDSNGVETFSCHTNHRIECAGYCYCLKGS 123

QY 121 AHAGFCLEHASCPGACVIAPGIPSONTCOPCPPTGFSASSSSECCQPHRNTALGLA 180

DB 124 SGCAKCVSQKRCGIGVY-SGHSTGTGVVCSPCGLGTYSHTVSSADKCEPVSTFMYNI 182

QY 181 LNVPGSSHDPLTCTSGTGFPLSTRVPGAE 209

DB 183 VEINLRYVNDTSCTRTTTTGLSESTSE 211

RESULT 14

TR14_HUMAN STANDARD; PRT; 283 AA.

ID TR14_HUMAN

AC Q92956; Q9UM65; Q96J31; Q8WXR1;

DT 16-OCT-2001 (Rel. 40, Created)

DT 16-OCT-2001 (Rel. 40, Last sequence update)

DT 15-JUN-2002 (Rel. 41, Last annotation update)

DE Tumor necrosis factor receptor superfamily member 14 precursor

DE (Herpesvirus entry mediator A) (Tumor necrosis factor receptor-like 2)

DE (TR2).

GN TNFRSF14 OR HVEM OR HVFA.

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.

OX NCBI_TaxID=9606;

RN [1]

RP SEQUENCE FROM N.A.

RC TISSUE=Cervical adenocarcinoma;

RA MEDLINE=97053782; PubMed=8898196;

RA Montgomerie R.I., Warner M.S., Lum B.J., Spear P.G.;

RT "Herpes simplex virus-1 entry into cells mediated by a novel member of

RT the TNF/NGF receptor family.";

RL Cell 87:427-436(1996).

RP [2]

RP SEQUENCE FROM N.A.

RX MEDLINE=97306336; PubMed=9162061;

RA Kwon B.S., Tan K.B., Ni J., Oh K.-O., Lee Z.H., Kim K.K., Kim Y.-J.,

RA Wang S., Gentz R., Yu G.-L., Harrop J., Lyn S.D., Silverman C.,

RA Porter T.G., Truneh A., Young P.R.;

RT "A newly identified member of the tumor necrosis factor receptor

RT superfamily with a wide tissue distribution and involvement in

RT lymphocyte activation.";

RL J Biol. Chem. 272:14272-14276(1997).

RN [3]

RP SEQUENCE FROM N.A.

RA Zhang W., Wan T., Gao X.;

RL Submitted (MAY-1999) to the EMBL/Genbank/DBJ databases.

RN [4]

RP SEQUENCE FROM N.A., AND VARIANTS ARG-17 AND ILE-241.

RA MEDLINE=21629477; PubMed=11756979;

RA Struyf F., Posavad C.M., Keyaerts E., Van Raest M., Corey L.,

RA Spear P.G.;

RT "Search for polymorphisms in the genes for herpesvirus entry mediator,

RT Nectin-1, and Nectin-2 in immune seronegative individuals.";

RL J Infect. Dis. 185:36-44(2002).

RN [5]

RP SEQUENCE FROM N.A.

RC TISSUE=Skin;

RA Strausberg R.;

RL Submitted (FEB-2001) to the EMBL/Genbank/DBJ databases.

RN [6]

RP X-RAY CRYSTALLOGRAPHY (2.65 ANGSTROMS) OF 39-200.

RA MEDLINE=21403268; PubMed=11511370;

RA Garfi A., Willis S.H., Whitbeck J.C., Krumenacher C., Cohen G.H.,

RA Eisenberg R.J., Wiley D.C.;

RT "Herpes simplex virus glycoprotein D bound to the human receptor

RT HveaA".

RL Mol. Cell 8:169-179(2001).

CC -1- FUNCTION: Receptor for TNFRSF14/LIGHT and homotrimeric

CC TNFRSF1/lymphotoxin-alpha. Involved in lymphocyte activation. Plays

CC an important role in HSV pathogenesis because it enhanced the

CC entry of several wildtype HSV strains of both serotypes into CHO

CC cells, and mediated HSV entry into activated human T cells.

CC -1- SUBCELLULAR LOCATION: Type I membrane protein (Probable).

CC -1- TISSUE SPECIFICITY: WIDELY EXPRESSED, WITH THE HIGHEST EXPRESSION

CC IN LONG, SPLEEN, AND THYMUS.

CC -1- SIMILARITY: CONTAINS 3 TNFR-CYS REPEATS.

CC

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CC -----

DR EMBL: U70321; AAB58354.1; -

DR EMBL: U81232; AAD00505.1; -

DR EMBL: AF153978; AAF75588.1; -

DR EMBL: AF373877; AAL47717.1; -

DR EMBL: AF373878; AAL47718.1; -

DR EMBL: BC002794; AAH02794.1; -

DR PDB: 1JMA; 26-SEP-01.

DR Genew; HGNC:11912; TNFRSF14.

DR MIM; 602746; -

DR InterPro: IPR001368; TNFR_c6.

DR Pfam: PF00020; TNFR_c6; 3.

DR PRODOM: PD000771; TNFR_c6; 1.

DR SMART: SM00208; TNFR; 3.

DR PROSITE: PS00652; TNFR_NGFR_1; 1.

DR PROSITE: PS50050; TNFR_NGFR_2; 2.

KW Receptor: Transmembrane; Glycoprotein; Repeat; Signal; Polymorphism;

KW 3D-structure.

FT SIGNAL 1 38 POTENTIAL.

FT CHAIN 39 283 TUMOR NECROSIS FACTOR RECEPTOR

FT DOMAIN 39 202 SUPERFAMILY MEMBER 14.

FT TRANSMEM 203 223 EXTRACELLULAR (POTENTIAL).

FT DOMAIN 224 283 CYTOPLASMIC (POTENTIAL).
 FT REPEAT 42 75 TNFR-CYS 1.
 FT REPEAT 78 119 TNFR-CYS 2.
 FT REPEAT 121 162 TNFR-CYS 3.
 FT DISULFID 42 53
 FT DISULFID 54 67
 FT DISULFID 57 75
 FT DISULFID 78 93
 FT DISULFID 96 111
 FT DISULFID 99 119
 FT DISULFID 121 138
 FT DISULFID 127 135
 FT CARBOHYD 110 110
 FT CARBOHYD 173 173
 FT VARIANT 17
 FT VARIANT 241
 FT VARIANT 241
 SQ SEQUENCE 283 AA; 30392 MW; 46CE13C2C70242C1 CRC64;
 Query Match 15.1%; Score 246; DB 1; Length 283;
 Best Local Similarity 35.4%; Pred. No. 2, 7e-12;
 Matches 69; Conservative 16; Mismatches 88; Indels 22; Gaps 8;

QY 7 PGLSLICLVLPAL--LPVAVRGVAETPTVPMWDAETGERLVCAQCPPTGYORPCR 63
 DB 16 PKTVDRLVLYLFELGAPCYAPALPSCKE-DEYP-----VGSE-CCPKCSPGYRVKACG 68
 QY 64 RQSPITCGPCPPRHYYQFNMYLER---CRKCNVLCGEREAREACATNHRACRCRTGFF 120
 DB 69 ELTGVCCEPCPPETTYAHNLGSKCLQCCMCDPAMGIR--ASNNCRTEANAVCGSPGHR 126
 QY 121 A-----HAGFCELEHASCPPGAGVIAPTSPNTOCCPCCPFSSASSSSSECCOPHRNC 174
 DB 127 CTYQDGDHCAACAGAVATSPGQGVQKGTESDQLQNCPPGFFS-PNGTLECCQHOTKC 185
 QY 175 TALGLALNPGSSSH 189
 DB 186 SWLVTRKAGAGTSSSH 200

RESULT 15
 TR1_HUMAN STANDARD; PRT; 616 AA.
 ID TR1_HUMAN
 AC Q9Y606;
 DT 16-OCT-2001 (Rel. 40, Created)
 DT 16-OCT-2001 (Rel. 40, Last sequence update)
 DT 15-JUN-2002 (Rel. 41, Last annotation update)
 DE Tumor necrosis factor receptor superfamily member 11A precursor
 DE (Receptor activator of NF-kB) (Osteoclast differentiation factor
 DE (Receptor) (ODFR).
 GN TNFRSF11A OR RANK.
 OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Homiidae; Homo.
 OC NCBI_TaxId=9606;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE-Dendritic cell;
 RX MEDLINE=98032977; PubMed=9367155;
 RA Anderson D.M., Maraskovsky E., Billingsley W.L., Dougal W.C.,
 RA Tometsko M.E., Roux E.R., Teepe M.C., Dubeose R.F., Cosman D.,
 RA Galibert L.;
 RT "A homologue of the TNF receptor and its ligand enhance T-cell growth
 RT and dendritic-cell function.";
 RL Nature 390:175-179 (1997).
 RN [2]
 RP FUNCTION.
 RX MEDLINE=99097247; PubMed=9878548;
 RA Nakagawa N., Kinoshita K., Yamaguchi K., Shima N., Yasuda H., Yano K.,
 RA Morinaga T., Higashio K.;
 RT "RANK is the essential signaling receptor for osteoclast
 RT differentiation factor in osteoclastogenesis.";

RL Biochem. Biophys. Res. Commun. 253:395-400 (1998).
 RN [3]
 RP VARIANT FEO 16-L-L-21 DUPL, VARIANT PDB2 13-A-L-21 DUPL, AND VARIANT
 RP V-192.
 RX MEDLINE=20082806; PubMed=10615125;
 RA Hughes A.E., Ralston S.H., Maiken J., Bell C., Macpherson H.,
 RA Wallace R.G.H., van Hul W., Whyte M.P., Nakatsuka K., Hovy L.,
 RA Anderson D.M.;
 RT "Mutations in TNFRSF11A, affecting the signal peptide of RANK, cause
 RT familial expansile osteolysis.";
 RL Nat. Genet. 24:45-48 (2000).
 CC -1- FUNCTION: Receptor for TNFRSF11/RANKL/OPGL; essential for
 CC RANKL-mediated osteoclastogenesis. Involved in the regulation of
 CC interactions between T-cells and dendritic cells.
 CC -1- SUBCELLULAR LOCATION: Type I membrane protein (Potential).
 CC -1- TISSUE SPECIFICITY: Ubiquitous expression with high levels in
 CC SKELETAL MUSCLE, THYMUS, LIVER, COLON, SMALL INTESTINE AND ADRENAL
 CC GLAND.
 CC -1- DISEASE: DEFECTS IN TNFRSF11 ARE THE CAUSE OF FAMILIAL EXPANSILE
 CC OSTEOLYSIS (FEO), A RARE AUTOSOMAL DOMINANT BONE DISORDER
 CC CHARACTERIZED BY FOCAL AREAS OF INCREASED BONE REMODELLING. THE
 CC OSTEOCLASTIC LESIONS DEVELOP USUALLY IN THE LONG BONES DURING EARLY
 CC ADULTHOOD. FEO IS OFTEN ASSOCIATED WITH EARLY ONSET DEAFNESS AND
 CC LOSS OF DENTITION.
 CC -1- DISEASE: DEFECTS IN TNFRSF11 ARE A CAUSE OF FAMILIAL PAGET
 CC DISEASE OF BONE, ALSO KNOWN AS PAGET DISEASE OF BONE 2 (PDB2). IT
 CC IS A BONE REMODELLING DISORDER WITH CLINICAL SIMILARITIES TO FEO.
 CC UNLIKE FEO, HOWEVER, AFFECTED INDIVIDUALS HAVE INVOLVEMENT OF THE
 CC AXIAL SKELETON WITH LESIONS IN THE SPINE, PELVIS AND SKULL.
 CC -1- SIMILARITY: CONTAINS 4 TNFR-CYS REPEATS.
 CC -----
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 CC -----
 DR EMBL: AF018253; AAB86809.1; -
 DR HSSP: P25942; ICDF.
 DR Genew; HGNC:11908; TNFRSF11A.
 DR MIM: 603499; -
 DR MIM: 174810; -
 DR MIM: 602080; -
 DR InterPro: IPR001368; TNFR_c6.
 DR Pfam: PF000020; TNFR_c6; 4.
 DR ProDom; PD000771; TNFR_c6; 1.
 DR SMART; SM00208; TNFR; 4.
 DR PROSITE; PS00652; TNFR_NGFR_1; 1.
 DR PROSITE; PS00650; TNFR_NGFR_2; 1.
 KW Receptor; Transmembrane; Glycoprotein; Repeat; Signal; Polymorphism;
 KW Disease mutation.
 FT SIGNAL 1 29
 FT CHAIN 30 616
 FT FT
 FT DOMAIN 30 212
 FT TRANSMEM 213 233
 FT DOMAIN 234 616
 FT REPEAT 34 68
 FT REPEAT 71 112
 FT REPEAT 114 151
 FT REPEAT 154 194
 FT DISULFID 34 46
 FT DISULFID 47 60
 FT DISULFID 50 68
 FT DISULFID 71 86
 FT DISULFID 92 112
 FT DISULFID 114 127
 FT DISULFID 133 151
 FT CARBOHYD 105 105
 FT CARBOHYD 174 174
 FT VARIANT 21 21

POTENTIAL.
 TUMOR NECROSIS FACTOR RECEPTOR
 SUPERFAMILY MEMBER 11A.
 EXTRACELLULAR (POTENTIAL).
 POTENTIAL.
 CYTOPLASMIC (POTENTIAL).
 TNFR-CYS 1.
 TNFR-CYS 2.
 TNFR-CYS 3.
 TNFR-CYS 4.
 BY SIMILARITY.
 BY SIMILARITY.
 BY SIMILARITY.
 BY SIMILARITY.
 BY SIMILARITY.
 BY SIMILARITY.
 N-LINKED (GLCNAC. . .) (POTENTIAL).
 N-LINKED (GLCNAC. . .) (POTENTIAL).
 L -> LALLLALL (IN PDB2).

RP SEQUENCE FROM N.A.
RC STRAIN-NOD;
RX MEDLINE-95178848; PubMed-7873884;
RA Powell E.E., Wicker L.S., Peterson L.B., Todd J.A.;
RT "Allelic variation of the type 2 tumor necrosis factor receptor
gene";
RL Mamm. Genome 5:726-727(1994).
DR EMBL; X76401; CAA53981.1; -.
DR HSSP; P19438; INCF.
DR MGD; MGI:1314883; Tnfrsf1b.
DR InterPro; IPR001368; TNFR_c6.
DR Pfam; PF00020; TNFR_c6; 4.
DR SMART; SM00208; TNFR; 4.
DR PROSITE; PS00652; TNFR_NGFR_1; 2.
DR PROSITE; PS50050; TNFR_NGFR_2; 3.
KM Receptor.
FT NON_TER 1 1
FT VARIANT 87 87 S -> T.
FT VARIANT 93 93 T -> I.
FT VARIANT 268 268 F -> I.
FT VARIANT 345 345 S -> F.
FT VARIANT 421 422 Y -> C.
SQ SEQUENCE 459 AA; 48686 MW; 6C51D2CF1C4626DF CRC64;
Query Match 20.4%; Score 333.5; DB 11; Length 459;
Best Local Similarity 29.7%; Pred. No. 6.4e-21;
Matches 81; Conservative 43; Mismatches 110; Indels 39; Gaps 9;
QY 46 RLVCACCPGTEVQVPCRRDPTGCPGPRHYTQFWNYLERCRYCNVLGGEREERARAC 105
DB 37 QMCCACPCPGQVYKHFCNKTSDFVACADCEASMTYQVWNOFRTCLSCSSCSTDQVETRRAC 96
QY 106 HATHNACRGRTEFF-----AHAGF-----CLEHASCPCGAGVIAGTFSQNTQCCPCTGTF 158
DB 97 TKQNNVCACEAGRYCALKTSHSGCRQMRLSKCGPFGVASSRAPGNVLCKACACGTF 156
QY 159 SASSSSEOCQPHRNCTALGLALNVPGSSSHDTLCT-----SCYGFPLSTRVPGAEBCERA 214
DB 157 SDTTSSTVDCRPHRISILA-----IPGNASTDAVCAPESTLTAIPRTLVSQPEPTRSQ 212
QY 215 VIDFVAFODISIKRLRLQALAPAGWGCTP-----RAGRAALQKLRRRLTELLGAQD 269
DB 213 PLD-----QERGPSQTSILSTL-----GSTPIEDSTKGISLIGLIVGVTSL----- 257
QY 270 GALLVRLQAL-----RVARMGGLERSVREERFLP 298
DB 258 GLIMLGLVNCFTLYVRKKKPSCLQDAKVPHP 290
RESULT 5
088734 PRELIMINARY; PRT; 482 AA.
AC 088734;
DT 01-NOV-1998 (TREMBLrel. 08, Created)
DT 01-NOV-1998 (TREMBLrel. 08, Last sequence update)
DT 01-JUN-2002 (TREMBLrel. 21, Last annotation update)
DE p80 TNF-alpha receptor;
GN TNFR2.
OS Mus musculus (mouse).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_TaxId=10090;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE-98414512; PubMed-9740674;
RA Hurler B., Segade F., Rodriguez R., Ramos S.S., Lazo P.S.;
RT "The Mouse Tumor Necrosis Factor Receptor 2 Gene: Genomic Structure
and Characterization of the two Transcripts";
RL Genomics 52:79-98(1998).
DR EMBL; Y14619; CAA74969.1; -.
DR EMBL; Y14620; CAA74969.1; JOINED.
DR EMBL; Y14621; CAA74969.1; JOINED.
DR EMBL; Y14622; CAA74969.1; JOINED.

DR EMBL; Y14623; CAA74969.1; JOINED.
DR EMBL; Y14679; CAA74969.1; JOINED.
DR HSSP; P19438; INCF.
DR InterPro; IPR001368; TNFR_c6.
DR Pfam; PF00020; TNFR_c6; 4.
DR SMART; SM00208; TNFR; 4.
DR PROSITE; PS00652; TNFR_NGFR_1; 2.
DR PROSITE; PS50050; TNFR_NGFR_2; 3.
KM Receptor.
SQ SEQUENCE 482 AA; 51106 MW; F6C15046B48FF83C CRC64;
Query Match 20.0%; Score 327; DB 11; Length 482;
Best Local Similarity 29.3%; Pred. No. 2.5e-20;
Matches 82; Conservative 43; Mismatches 109; Indels 46; Gaps 10;
QY 46 RLVCACCPGTEVQVPCRR-----DSPITTCGCPGPRHYTQFWNYLERCRYCNVLGGER 98
DB 52 QMCCACPCPGQVYKHFCNKTSDFVACADCEASMTYQVWNOFRTCLSCSSCSTD 111
QY 99 EEEARACHATHNACRGRTEFF-----AHAGF-----CLEHASCPCGAGVIAGTFSQNTQCC 151
DB 112 QVETRACTQKQNNVCACEAGRYCALKTSHSGCRQMRLSKCGPFGVASSRAPGNVLCK 171
QY 152 PCPEGTFSASSSEOCQPHRNCTALGLALNVPGSSSHDTLCT-----SCYGFPLSTRVPG 207
DB 172 ACAPGTFSDTSSDVCRPHRISILA-----IPGNASTDAVCAPESTLTAIPRTLVSQ 227
QY 208 AEBCERAVIDFVAFODISIKRLRLQALAPAGWGCTP-----RAGRAALQKLRRRLT 262
DB 228 PEPTRSQPLD-----QERGPSQTSILSTL-----GSTPIEDSTKGISLIGLIVGVT 277
QY 263 ELIAGADGALLVRLQAL-----RVARMGGLERSVREERFLP 298
DB 278 SL-----GLIMLGLVNCFTLYVRKKKPSCLQDAKVPHP 312
RESULT 6
0912M6 PRELIMINARY; PRT; 433 AA.
AC 0912M6;
DT 01-DEC-2001 (TREMBLrel. 19, Created)
DT 01-DEC-2001 (TREMBLrel. 19, Last sequence update)
DT 01-MAR-2002 (TREMBLrel. 20, Last annotation update)
DE Tumor necrosis factor receptor type II (Fragment).
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_TaxId=10116;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN-SPRAGUE-DAWLEY;
RA Osburg B., Peiser C., Doemling D., Schomburg L., Voigt K., Bickel U.;
RT "TNF-receptors p60 and p80 are constitutively expressed by rat brain
capillary endothelial cells and participate in TNF-alpha transport
through the blood-brain barrier";
RL Submitted (SEP-2001) to the EMBL/GenBank/DBJ databases.
DR EMBL; AF420214; AAL16021.1; -.
DR InterPro; IPR001368; TNFR_c6.
DR Pfam; PF00020; TNFR_c6; 4.
DR PROSITE; PS00652; TNFR_NGFR_1; UNKNOWN_2.
DR PROSITE; PS50050; TNFR_NGFR_2; 3.
KM Receptor.
FT NON_TER 1 1
FT VARIANT 433 433
SQ SEQUENCE 433 AA; 45723 MW; 75736D835E72CA4A CRC64;
Query Match 19.2%; Score 313.5; DB 11; Length 433;
Best Local Similarity 35.1%; Pred. No. 3.3e-19;
Matches 59; Conservative 29; Mismatches 67; Indels 13; Gaps 4;
QY 46 RLVCACCPGTEVQVPCRRDPTGCPGPRHYTQFWNYLERCRYCNVLGGEREERARAC 105
DB 32 QMCCACPCPGQVYKHFCNKTSDFVACADCAAGMTYQVWNIHTCLSCSSCSDQVETRRNC 91

RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN-ZAIRE-1979:
RA Loparev V.N., Parsons J.M., Esposito J.J.:
RT "DNA sequence analysis as a criterion for allocation of the
RT orthopoxviruses to a particular species."
RL Submitted (JAN-1997) to the EMBL/GenBank/DBJ databases.
DR EMBL: U87847; AAB94364.1; -
DR HSSP: 014763; 1D0G.
DR InterPro: IPR001368; TNFR_c6.
DR Pfam: PF00020; TNFR_c6; 2.
DR SMART: SM00208; TNFR_2.
DR PROSITE: PS00652; TNFR_NGFR_1; 2.
DR PROSITE: PS50050; TNFR_NGFR_2; 2.
KW Receptor.
SQ SEQUENCE 348 AA; 38184 MW; 34A5E668B27907B5 CRC64;

Query Match 17.2%; Score 280.5; DB 12; Length 348;
Best Local Similarity 30.4%; Pred. No. 1.9e-16;
Matches 63; Conservative 34; Mismatches 97; Indels 13; Gaps 3;

QY 9 LSLICLVLPALPLPVAIVGVAETPTTWMRDAGTEGRLVCAQCPPTGTVQAPCRDSDPT 68
DB 10 LFLSCITINGRDIAPAPNSGKCKDNEYRSRN-----LCCLSCPPGTASRLCDSTWT 63
QY 69 TCGPCPPRHVYQFWNTLERCRCYCNVLCGEEREEARACHATHNRACRCRTGFF-----AH 122
DB 64 QCTPCGSDPTFTSHNHQACLSGCRGDSNQVETRSCNTTHNRICGSPGYCYLLGSSG 123
QY 123 AGFCLHASCPPGAGVIAPGTPTSONTOCCPPGPTFSASSSSSEOCOPHRNCTALGLALN 182
DB 124 CRTICSKTKGIGYGV-SGYTSGDVICSPCGGTYSHVTSYSDKCEPVTSTNFTYIDVE 182
QY 183 VPGSSSHDILCTSCGTGFPPLSTRVPGA 209
DB 183 INLYPVNDISCTRTTTTGLSEISTSE 209

RESULT 10

057108 PRELIMINARY; PRT; 348 AA.
AC 057108;
DT 01-JUN-1998 (TREMBLrel. 06, Created)
DT 01-JUN-1998 (TREMBLrel. 06, Last sequence update)
DT 01-JUN-2002 (TREMBLrel. 21, Last annotation update)
DE Tumor necrosis factor receptor II homolog.
GN CRMB.
OS Monkeypox virus.
OC Viruses; dsDNA viruses, no RNA stage; Poxviridae; Chordopoxvirinae;
OC Orthopoxvirus.
OX NCBI_TaxID=10244;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN-ZAIRE-1970:
RA Loparev V.N., Parsons J.M., Esposito J.J.:
RT "DNA sequence analysis as a criterion for allocation of the
RT orthopoxviruses to a particular species."
RL Submitted (FEB-1997) to the EMBL/GenBank/DBJ databases.
DR EMBL: U88142; AAB94367.1; -
DR HSSP: 014763; 1D0G.
DR InterPro: IPR001368; TNFR_c6.
DR Pfam: PF00020; TNFR_c6; 2.
DR SMART: SM00208; TNFR_2.
DR PROSITE: PS00652; TNFR_NGFR_1; 2.
DR PROSITE: PS50050; TNFR_NGFR_2; 2.
KW Receptor.
SQ SEQUENCE 348 AA; 38212 MW; E555979057DEC91F CRC64;

Query Match 17.2%; Score 280.5; DB 12; Length 348;
Best Local Similarity 30.4%; Pred. No. 1.9e-16;
Matches 63; Conservative 34; Mismatches 97; Indels 13; Gaps 3;
QY 9 LSLICLVLPALPLPVAIVGVAETPTTWMRDAGTEGRLVCAQCPPTGTVQAPCRDSDPT 68

DB 10 LFLSCITINGRDIAPAPNSGKCKDNEYRSRN-----LCCLSCPPGTASRLCDSTWT 63
QY 69 TCGPCPPRHVYQFWNTLERCRCYCNVLCGEEREEARACHATHNRACRCRTGFF-----AH 122
DB 64 QCTPCGSDPTFTSHNHQACLSGCRGDSNQVETRSCNTTHNRICGSPGYCYLLGSSG 123
QY 123 AGFCLHASCPPGAGVIAPGTPTSONTOCCPPGPTFSASSSSSEOCOPHRNCTALGLALN 182
DB 124 CRTICSKTKGIGYGV-SGYTSGDVICSPCGGTYSHVTSYSDKCEPVTSTNFTYIDVE 182
QY 183 VPGSSSHDILCTSCGTGFPPLSTRVPGA 209
DB 183 INLYPVNDISCTRTTTTGLSEISTSE 209

RESULT 11

057100 PRELIMINARY; PRT; 349 AA.
AC 057100;
DT 01-JUN-1998 (TREMBLrel. 06, Created)
DT 01-JUN-1998 (TREMBLrel. 06, Last sequence update)
DT 01-JUN-2002 (TREMBLrel. 21, Last annotation update)
DE Tumor necrosis factor receptor II homolog.
GN CRMB.
OS Monkeypox virus.
OC Viruses; dsDNA viruses, no RNA stage; Poxviridae; Chordopoxvirinae;
OC Orthopoxvirus.
OX NCBI_TaxID=10244;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN-NIGERIA-1971:
RA Loparev V.N., Parsons J.M., Esposito J.J.:
RT "DNA sequence analysis as a criterion for allocation of the
RT orthopoxviruses to a particular species."
RL Submitted (JAN-1997) to the EMBL/GenBank/DBJ databases.
DR EMBL: U87844; AAB94361.1; -
DR HSSP: 014763; 1D0G.
DR InterPro: IPR001368; TNFR_c6.
DR Pfam: PF00020; TNFR_c6; 2.
DR SMART: SM00208; TNFR_2.
DR PROSITE: PS00652; TNFR_NGFR_1; 2.
DR PROSITE: PS50050; TNFR_NGFR_2; 2.
KW Receptor.
SQ SEQUENCE 349 AA; 38239 MW; DF6C280D478F2422 CRC64;

Query Match 16.9%; Score 276; DB 12; Length 349;
Best Local Similarity 30.0%; Pred. No. 4.6e-16;
Matches 63; Conservative 34; Mismatches 95; Indels 18; Gaps 5;

QY 9 LSLICLVLPALPLPVAIVGVAETPTTWMRDAGTEGRLVCAQCPPTGTVQAPCRDSDPT 68
DB 10 LFLSCITINGRDIAPAPNSGKCKDNEYRSRN-----LCCLSCPPGTASRLCDSTWT 63
QY 69 TCGPCPPRHVYQFWNTLERCRCYCNVLCGEEREEARACHATHNRACRCRTGFF-----AH 122
DB 64 QCTPCGSDPTFTSHNHQACLSGCRGDSNQVETRSCNTTHNRICGSPGYCYLLGSSG 123
QY 123 AGFCLHASCPPGAGVIAPGTPTSONTOCCPPGPTFSASSSSSEOCOP--HRNCTALGL 179
DB 124 CRTICSKTKGIGYGV-SGYTSGDVICSPCGGTYSHVTSYSDKCEPVTSTNFTYIDVE 182
QY 180 ALNVPSSSHDILCTSCGTGFPPLSTRVPGA 209
DB 183 EINL--YPVNDISCTRTTTTGLSEISTSE 210

RESULT 12

057101 PRELIMINARY; PRT; 349 AA.
AC 057101;
DT 01-JUN-1998 (TREMBLrel. 06, Created)
DT 01-JUN-1998 (TREMBLrel. 06, Last sequence update)

DT 01-JUN-2002 (TREMBLrel. 21, last annotation update)
 DE Tumor necrosis factor receptor II homolog.
 GN CRMB.
 OS Monkeypox virus.
 OC Viruses; dsDNA viruses, no RNA stage; Poxviridae; Chordopoxvirinae;
 OC Orthopoxvirus.
 OX NCBI_TaxId=10244;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC STRAIN-ZAIRE-1977;
 RA Loparev V.N., Parsons J.M., Esposito J.J.;
 RT "DNA sequence analysis as a criterion for allocation of the
 RT orthopoxviruses to a particular species";
 RL Submitted (JAN-1997) to the EMBL/GenBank/DBJ databases.
 DR EMBL: U87845; AAB94362.1; -
 DR HSSP: 014763; 1DOG.
 DR InterPro: IPR001368; TNR_C6.
 DR Pfam: PF00020; TNR_C6; 2.
 DR SMART: SM00208; TNR_2.
 DR PROSITE: PS00652; TNR_NGFR_1; 2.
 DR PROSITE: PS50050; TNR_NGFR_2; 2.
 KM Receptor.
 SQ SEQUENCE 349 AA; 38311 MW; 02F65B00CFB858BE CRC64;

Query Match 16.8%; Score 274; DB 12; Length 349;
 Best Local Similarity 30.0%; Pred. No. 6.9e-16;
 Matches 63; Conservative 34; Mismatches 95; Indels 18; Gaps 5;

OY 9 LSLCLVIALPALLPVPAVGVAEPTPTWMDAETGERLYCAQCPGTFVORPCRRDSPT 68
 DB 10 LFLSCIITINGRDIAHAPSNGKCKDNEYRSR-----LCCLSCPGTYASRLCDSKNT 63
 OY 69 TCGPCPPRHYYQFMWYLERCRVCNVLGGEREEARACHATNRACRGTGFF-----AH 122
 DB 64 OCTPGSGDTFTSHNNHLQACLSNCRCSNOVETRSCHTNRHRCESPGYICLLKGSAG 123
 OY 123 AGFCLHASCPCPGAVIAGTPSNTQCPCPGTFSSASSSSSEOCQ---HRNCTALGL 179
 DB 124 CRTCISKTKCGIGYGV-SGYTSTGDTVICSPCGPGTYSHTVSSTDKCEPVVTSNFTNYIDV 182
 OY 180 ALNVPGSSSHDTLCTSCGTGFPPLSTRVPGA 209
 DB 183 EITNL--YPVNDTSCRTTTTGLSEISITSE 210

RESULT 13

057102 PRELIMINARY; PRT; 349 AA.

AC 057102;
 DT 01-JUN-1998 (TREMBLrel. 06, Created)
 DT 01-JUN-1998 (TREMBLrel. 06, last sequence update)
 DT 01-JUN-2002 (TREMBLrel. 21, last annotation update)
 DE Tumor necrosis factor receptor II homolog.
 GN CRMB.
 OS Monkeypox virus.
 OC Viruses; dsDNA viruses, no RNA stage; Poxviridae; Chordopoxvirinae;
 OC Orthopoxvirus.
 OX NCBI_TaxId=10244;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC STRAIN-BENIN-1978;
 RA Loparev V.N., Parsons J.M., Esposito J.J.;
 RT "DNA sequence analysis as a criterion for allocation of the
 RT orthopoxviruses to a particular species";
 RL Submitted (JAN-1997) to the EMBL/GenBank/DBJ databases.
 DR EMBL: U87846; AAB94363.1; -
 DR HSSP: 014763; 1DOG.
 DR InterPro: IPR001368; TNR_C6.
 DR Pfam: PF00020; TNR_C6; 2.
 DR SMART: SM00208; TNR_2.
 DR PROSITE: PS00652; TNR_NGFR_1; 2.
 DR PROSITE: PS50050; TNR_NGFR_2; 2.
 KM Receptor.

SQ SEQUENCE 349 AA; 38308 MW; CBD2C949E994C59C CRC64;

Query Match 16.8%; Score 274; DB 12; Length 349;
 Best Local Similarity 30.0%; Pred. No. 6.9e-16;
 Matches 63; Conservative 34; Mismatches 95; Indels 18; Gaps 5;

OY 9 LSLCLVIALPALLPVPAVGVAEPTPTWMDAETGERLYCAQCPGTFVORPCRRDSPT 68
 DB 10 LFLSCIITINGRDIAHAPSNGKCKDNEYRSR-----LCCLSCPGTYASRLCDSKNT 63
 OY 69 TCGPCPPRHYYQFMWYLERCRVCNVLGGEREEARACHATNRACRGTGFF-----AH 122
 DB 64 OCTPGSGDTFTSHNNHLQACLSNCRCSNOVETRSCHTNRHRCESPGYICLLKGSAG 123
 OY 123 AGFCLHASCPCPGAVIAGTPSNTQCPCPGTFSSASSSSSEOCQ---HRNCTALGL 179
 DB 124 CRTCISKTKCGIGYGV-SGYTSTGDTVICSPCGPGTYSHTVSSTDKCEPVVTSNFTNYIDV 182
 OY 180 ALNVPGSSSHDTLCTSCGTGFPPLSTRVPGA 209
 DB 183 EITNL--YPVNDTSCRTTTTGLSEISITSE 210

RESULT 14

057291 PRELIMINARY; PRT; 349 AA.

DT 01-JUN-1998 (TREMBLrel. 06, Created)
 DT 01-JUN-1998 (TREMBLrel. 06, last sequence update)
 DT 01-JUN-2002 (TREMBLrel. 21, last annotation update)
 DE Tumor necrosis factor receptor II homolog.
 GN CRMB.
 OS Monkeypox virus.
 OC Viruses; dsDNA viruses, no RNA stage; Poxviridae; Chordopoxvirinae;
 OC Orthopoxvirus.
 OX NCBI_TaxId=10244;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC STRAIN-VARIOUS STRAINS;
 RA Loparev V.N., Parsons J.M., Esposito J.J.;
 RL Submitted (JAN-1998) to the EMBL/GenBank/DBJ databases.
 DR EMBL: U88144; AAB94369.1; -
 DR EMBL: U87842; AAB94359.1; -
 DR EMBL: U87994; AAB94365.1; -
 DR EMBL: U87995; AAB94366.1; -
 DR EMBL: U88143; AAB94368.1; -
 DR HSSP: 014763; 1DOG.
 DR InterPro: IPR001368; TNR_C6.
 DR Pfam: PF00020; TNR_C6; 2.
 DR SMART: SM00208; TNR_2.
 DR PROSITE: PS00652; TNR_NGFR_1; 2.
 DR PROSITE: PS50050; TNR_NGFR_2; 2.
 SQ SEQUENCE 349 AA; 38295 MW; CBD2C949ED2B8E7C CRC64;

Query Match 16.8%; Score 274; DB 12; Length 349;
 Best Local Similarity 30.0%; Pred. No. 6.9e-16;
 Matches 63; Conservative 34; Mismatches 95; Indels 18; Gaps 5;

OY 9 LSLCLVIALPALLPVPAVGVAEPTPTWMDAETGERLYCAQCPGTFVORPCRRDSPT 68
 DB 10 LFLSCIITINGRDIAHAPSNGKCKDNEYRSR-----LCCLSCPGTYASRLCDSKNT 63
 OY 69 TCGPCPPRHYYQFMWYLERCRVCNVLGGEREEARACHATNRACRGTGFF-----AH 122
 DB 64 OCTPGSGDTFTSHNNHLQACLSNCRCSNOVETRSCHTNRHRCESPGYICLLKGSAG 123
 OY 123 AGFCLHASCPCPGAVIAGTPSNTQCPCPGTFSSASSSSSEOCQ---HRNCTALGL 179
 DB 124 CRTCISKTKCGIGYGV-SGYTSTGDTVICSPCGPGTYSHTVSSTDKCEPVVTSNFTNYIDV 182
 OY 180 ALNVPGSSSHDTLCTSCGTGFPPLSTRVPGA 209
 DB 183 EITNL--YPVNDTSCRTTTTGLSEISITSE 210

RESULT 15

057099

ID 057099 PRELIMINARY; PRT; 349 AA.

AC 057099;

DT 01-JUN-1998 (TReMBLrel. 06, Created)

DT 01-JUN-1998 (TReMBLrel. 06, last sequence update)

DT 01-JUN-2002 (TReMBLrel. 21, last annotation update)

DE Tumor necrosis factor receptor II homolog.

GN CRMB.

OS Monkeypox virus.

OC Viruses; dsDNA viruses, no RNA stage; Poxviridae; Chordopoxvirinae;

OC Orthopoxvirus.

OX NCBI_TaxID-10244;

RN [1]

RP SEQUENCE FROM N.A.

RC STRAIN-SIERRA LEONE-1970;

RA Loparev V.N., Parsons J.M., Esposito J.J.;

RT "DNA sequence analysis as a criterion for allocation of the

RT orthopoxviruses to a particular species."

RL Submitted (JAN-1997) to the EMBL/GenBank/DBJ databases.

DR EMBL; U87843; AAB94360.1; .

DR HSSP; O14763; IDOG.

DR InterPro; IPR001368; TNFR_c6.

DR Pfam; PF00020; TNFR_c6; 2.

DR SMART; SM00208; TNFR; 2.

DR PROSITE; PS00652; TNFR_NGFR_1; 2.

DR PROSITE; PS50050; TNFR_NGFR_2; 2.

KM Receptor.

SQ SEQUENCE 349 AA; 38321 MW; FE449028C933FE7 CRC64;

Query Match 16.7%; Score 273; DB 12; Length 349;

Best Local Similarity 30.0%; Pred. No. 8,4e-16;

Matches 63; Conservative 33; Mismatches 96; Indels 18; Gaps 5;

QY 9 LSLICLVLPALPVPVAVRGVAETPTYPWRDAETGERLVCAOCPGTFVQRPGRDPT 68

Db 10 LFLSCIIINGRDIAFHAPSGKCKDNEYRSN-----LCCLSCPPTIASRLCDSKNT 63

QY 69 TCGPCPPRHAYTOFWNYLERCRVCNVLCGEREEEARACHATNHRACRGTGFFA-----H 122

Db 64 QCTPGCGSDFTSHNNHLDQACLSGRCDSNOVETRSCNTNHRICEGSPGYCCLKGALG 123

QY 123 AGCLLEHASCPPGAGVYAPGTPOSONTOCQPCPGTSSASSSSSEQCOP---HRNCTALGL 179

Db 124 CRTGISRTKCGIGYV-SGYTSTGVDYISPCGPGTSHYVSSFDKCEPVVTSNTFNVIDV 182

QY 180 ALNVPSSSHDTLCTSGTGFPLSTRVPGAE 209

Db 183 EINDL--YPVNDTSCRTTTTGTGLSEISTSE 210

Search completed: July 16, 2003, 19:38:58
Job time : 83 secs

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: July 16, 2003, 19:37:04 ; Search time 38 Seconds
(without alignments)
1051.979 Million cell updates/sec

Title: US-09-935-727-2

Perfect score: 300
Sequence: 1 MNALEGPGLSLICLVIALPA.....RVARMPGLERSVRERLPVH 300

Scoring table: OLIGO
Gapop 60.0 , Gapept 60.0

Searched: 908470 seqs, 133250620 residues

Word size : 0

Total number of hits satisfying chosen parameters: 908470

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Listing first 45 summaries

Database :

A.Geneseq..101002.*
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22: /SID2/gcgdata/geneseq/genesqp-emb1/AA2001.DAT:*
23: /SID2/gcgdata/geneseq/genesqp-emb1/AA2002.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | Query Match | Length | ID | Description |
|------------|-------|-------------|--------|----|-------------|
| 1 | 300 | 100.0 | 300 | 19 | AAW66102 |
| 2 | 300 | 100.0 | 300 | 19 | AAW63622 |
| 3 | 300 | 100.0 | 300 | 20 | AAV03099 |
| 4 | 300 | 100.0 | 300 | 20 | AAV42182 |
| 5 | 300 | 100.0 | 300 | 20 | AAV17479 |
| 6 | 300 | 100.0 | 300 | 20 | AAV06817 |
| 7 | 300 | 100.0 | 300 | 20 | AAW97749 |
| 8 | 300 | 100.0 | 300 | 20 | AAW95082 |
| 9 | 300 | 100.0 | 300 | 21 | AAI19335 |
| 10 | 300 | 100.0 | 300 | 21 | AAW28559 |

| | | | | | |
|----|-----|-------|-----|----|----------|
| 11 | 300 | 100.0 | 300 | 21 | AAW24057 |
| 12 | 300 | 100.0 | 300 | 21 | AAW33416 |
| 13 | 300 | 100.0 | 300 | 21 | AAW03621 |
| 14 | 300 | 100.0 | 300 | 21 | AAV97246 |
| 15 | 300 | 100.0 | 300 | 21 | AAV90357 |
| 16 | 300 | 100.0 | 300 | 21 | AAW24395 |
| 17 | 300 | 100.0 | 300 | 21 | AAV96596 |
| 18 | 300 | 100.0 | 300 | 22 | AAW03568 |
| 19 | 300 | 100.0 | 300 | 22 | AAW74466 |
| 20 | 300 | 100.0 | 300 | 22 | AAW71754 |
| 21 | 300 | 100.0 | 300 | 22 | AAW48161 |
| 22 | 300 | 100.0 | 300 | 22 | AAW50903 |
| 23 | 300 | 100.0 | 300 | 22 | AAE14579 |
| 24 | 300 | 100.0 | 300 | 22 | AAE20848 |
| 25 | 300 | 100.0 | 300 | 22 | AAW73740 |
| 26 | 279 | 93.0 | 326 | 23 | AAW41980 |
| 27 | 271 | 90.3 | 271 | 20 | AAV42184 |
| 28 | 271 | 90.3 | 271 | 21 | AAW19334 |
| 29 | 271 | 90.3 | 271 | 21 | AAW19705 |
| 30 | 271 | 90.3 | 271 | 21 | AAV97247 |
| 31 | 271 | 90.3 | 271 | 21 | AAV96598 |
| 32 | 271 | 90.3 | 271 | 22 | AAW03567 |
| 33 | 271 | 90.3 | 271 | 22 | AAW68044 |
| 34 | 271 | 90.3 | 271 | 22 | AAW68047 |
| 35 | 271 | 90.3 | 271 | 22 | AAW74465 |
| 36 | 271 | 90.3 | 271 | 23 | AAE14578 |
| 37 | 240 | 80.0 | 245 | 20 | AAW28449 |
| 38 | 217 | 72.3 | 271 | 21 | AAW19709 |
| 39 | 217 | 72.3 | 271 | 22 | AAW03571 |
| 40 | 217 | 72.3 | 271 | 22 | AAW03584 |
| 41 | 217 | 72.3 | 271 | 22 | AAW74467 |
| 42 | 217 | 72.3 | 271 | 23 | AAE14581 |
| 43 | 217 | 72.3 | 271 | 23 | AAE14582 |
| 44 | 217 | 72.3 | 271 | 23 | AAE14584 |
| 45 | 217 | 72.3 | 271 | 23 | AAE14585 |

ALIGNMENTS

| | | |
|----------|--|--|
| RESULT 1 | AAW66102 | AAW66102 standard; Protein; 300 AA. |
| ID | AAW66102 | |
| XX | | |
| AC | AAW66102: | |
| XX | | |
| DT | 02-DEC-1998 | (first entry) |
| XX | | |
| DE | | Amino acid sequence of tumour necrosis related receptor (TR4). |
| XX | | |
| KW | Human; tumour necrosis related receptor; TR4; agonist; antagonist; | |
| KW | Inhibition; Chronic; acute; Inflammation; arthritis; septicemia; | |
| KW | Autoimmune disease; transplant rejection; stroke; cancer; | |
| KW | Alzheimer's disease. | |
| XX | | |
| OS | Homo sapiens. | |
| XX | | |
| PN | EP861850-A1. | |
| XX | | |
| PD | 02-SEP-1998. | |
| XX | | |
| PF | 20-JAN-1998; | 98EP-0300382. |
| XX | | |
| PR | 04-FEB-1997; | 97US-0794796. |
| XX | | |
| PA | (SMK) SMITHKLINE BEECHAM CORP. | |
| XX | | |
| PI | Emery J, Tan KB, Truneh A, Young PR; | |
| XX | | |
| DR | WPI; 1998-508248/44. | |
| XX | | |
| DR | N-PSDB; AAV07654. | |
| XX | | |
| PT | New DNA encoding tumour necrosis related receptor - used to treat | |

PT and prevent e.g. inflammation, arthritis, septicemia, autoimmune
PT diseases, transplant rejection, infection, stroke, ischaemia, ARDS,
PT restenosis, AIDS, bone disorders and cancer

PS Claim 1: Fig 1: 21pp: English.

XX This is the amino acid sequence of the human tumour necrosis related
CC receptor (TR4), used in the method of the invention. The TR4 protein
CC or its agonist can be used to treat a subject in need of enhanced
CC TR4 polypeptide activity. The antagonist is used to inhibit TR4
CC polypeptide activity. The active agents can be used for the
CC treatment and prevention of diseases such as chronic and acute
CC inflammation, arthritis, septicemia, autoimmune diseases, transplant
CC rejection, stroke, cancer, Alzheimer's disease.

CC Sequence 300 AA;

Query Match 100.0%; Score 300; DB 19; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.6e-269;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALGPGSLSLCLVIALPALPVPVAVGVATPTYPMDATGRLVCAOCPGTFYOR 60
DB 1 MRALGPGSLSLCLVIALPALPVPVAVGVATPTYPMDATGRLVCAOCPGTFYOR 60
QY 61 PCRRDSPPTGCGPPRRHYTOFWNLYLERCYCNVLGGEREEARACHATHNRACRGTGFF 120
DB 61 PCRRDSPPTGCGPPRRHYTOFWNLYLERCYCNVLGGEREEARACHATHNRACRGTGFF 120
QY 121 AHAGFCLHASCPPAGVYAPCTPSQNTQCCPPGTSASSSSSECCPHNCTALGIA 180
DB 121 AHAGFCLHASCPPAGVYAPCTPSQNTQCCPPGTSASSSSSECCPHNCTALGIA 180
QY 181 LNVPGSSSHDILCTCTGTFPLSTRVPGAECERAVIDYAFODISIKRLQRLQLEAPE 240
DB 181 LNVPGSSSHDILCTCTGTFPLSTRVPGAECERAVIDYAFODISIKRLQRLQLEAPE 240
QY 241 GNGPPTPRAGRALQKLRRLTELGAODGALLVRLQALRVARMPEGLERSYRERFLPVH 300
DB 241 GNGPPTPRAGRALQKLRRLTELGAODGALLVRLQALRVARMPEGLERSYRERFLPVH 300

RESULT 2
AAM63622
ID AAM63622 standard; Protein; 300 AA.

AC AAM63622;
XX 26-OCT-1998 (first entry)
DT Human tumour necrosis factor receptor-6 alpha protein.
XX Human tumour necrosis factor receptor-6 alpha protein.
DE Human tumour necrosis factor receptor-6 alpha; TNFR-6 alpha; TNFR-6 beta;
XX endotheial cells; keratinocytes; normal prostate; apoptosis;
KM prostate tumour tissue.
KM Homo sapiens.

OS Homo sapiens.
XX Key Location/Qualifiers
FH Peptide 1..30
FT Protein 31..300
FT /note="TNFR-6 alpha"
FT /note="Soluble extracellular domain"

XX Region
XX WO9830694-A2.
XX 16-JUL-1998.
XX 13-JAN-1998; 98WO-US00153.
XX 14-JAN-1997; 97US-0035496.

PA (HUMA-) HUMAN GENOME SCI INC.

XX Ebner R, Feng P, Gentz RL, Ni J, Ruben SM, Yu G;

XX WPI: 1998-399142/34.
DR N-PSDB: AAY39085.

PT Human tumour necrosis factor receptors 6-alpha and 6-beta - used in
PT the diagnosis of immune system-related disorder(s)
PS Claim 20; Fig 1; 91pp: English.

XX The present sequence represents the human tumour necrosis factor
CC receptor-6 alpha (TNFR-6 alpha) protein. The invention also provides
CC for the TNFR-6 beta protein (AAM63623). TNFR-6 alpha and TNFR-6 beta
CC are members of the tumour necrosis factor receptor (TNFR) family. TNFRs
CC are expressed in endothelial cells, keratinocytes, normal prostate and
CC prostate tumour tissue. For a number of disorders of these cells,
CC particularly of the immune system, substantially altered (whether
CC increased or decreased) levels of TNFR-6 alpha and/or TNFR-6 beta gene
CC expression can be detected, therefore the TNFR-6 alpha and TNFR-6 beta
CC polypeptides, nucleic acids and antibodies are claimed to be useful in
CC the diagnosis of such disorders. Mutations of the TNFR-6 alpha and
CC TNFR-6 beta genes can also be detected. The TNFR polypeptides are
CC also claimed to be useful for identifying ligands which may be useful
CC in the treatment of apoptosis related disorders.

CC Sequence 300 AA;

Query Match 100.0%; Score 300; DB 19; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.6e-269;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALGPGSLSLCLVIALPALPVPVAVGVATPTYPMDATGRLVCAOCPGTFYOR 60
DB 1 MRALGPGSLSLCLVIALPALPVPVAVGVATPTYPMDATGRLVCAOCPGTFYOR 60
QY 61 PCRRDSPPTGCGPPRRHYTOFWNLYLERCYCNVLGGEREEARACHATHNRACRGTGFF 120
DB 61 PCRRDSPPTGCGPPRRHYTOFWNLYLERCYCNVLGGEREEARACHATHNRACRGTGFF 120
QY 121 AHAGFCLHASCPPAGVYAPCTPSQNTQCCPPGTSASSSSSECCPHNCTALGIA 180
DB 121 AHAGFCLHASCPPAGVYAPCTPSQNTQCCPPGTSASSSSSECCPHNCTALGIA 180
QY 181 LNVPGSSSHDILCTCTGTFPLSTRVPGAECERAVIDYAFODISIKRLQRLQLEAPE 240
DB 181 LNVPGSSSHDILCTCTGTFPLSTRVPGAECERAVIDYAFODISIKRLQRLQLEAPE 240
QY 241 GNGPPTPRAGRALQKLRRLTELGAODGALLVRLQALRVARMPEGLERSYRERFLPVH 300
DB 241 GNGPPTPRAGRALQKLRRLTELGAODGALLVRLQALRVARMPEGLERSYRERFLPVH 300

RESULT 3
AAY03099
ID AAY03099 standard; Protein; 300 AA.

AC AAY03099;
XX 09-DEC-1999 (first entry)
DT Human lung TNF-receptor protein.
XX Human lung TNF-receptor protein.

DE Tumour necrosis factor; TNF; TNF receptor; human; lung; gene therapy;
XX detection; immunoassay; diagnosis; disease; immune system; tumour;
KW osteogenic system; cardiovascular system; central nervous system; asthma;
KW peripheral nervous system; transplant incompatibility; antitumor;
KW rheumatoid arthritis; antiasthmatic; antiarthritic.

OS Homo sapiens.
XX Key Location/Qualifiers
FH

```

FT CDS 134..1036
FT /tag= a
FT /product= "TNF-receptor"
PN DE19809978-A1.
PD 16-SEP-1999.
XX
XX
XX 09-MAR-1998; 98DE-1009978.
XX
XX 09-MAR-1998; 98DE-1009978.
XX
XX (BADI ) BASF AG.
XX
XX
XX Kroeger B;
XX
XX WPI; 1999-519473/44.
XX N-PSDB; AA209998.
XX
XX New soluble member of tumor necrosis factor receptor family, useful for
XX identification specific modulators and for treating disease e.g. tumors
XX
XX Claim 1; Page 8-9; 10pp; German.
XX
XX This invention describes a novel tumor necrosis factor (TNF) receptor
XX (I) isolated from human lung tissue. (I) is used: (i) to raise specific
XX antibodies (Ab); (ii) to screen for specific (ant)agonists or ligands
XX (A), potential therapeutic agents; and (iii) therapeutically (optionally
XX expressed from a gene therapy vector) in conditions associated with a
XX deficit of (I). Ab are used: (a) for qualitative or quantitative
XX detection of (I) in standard immunoassays (for diagnosis of disease, or
XX susceptibility, or for monitoring); and (b) as therapeutic inhibitors in
XX cases where (I) is overexpressed. Nucleic acid (II) that encodes (I) is
XX used: (A) for recombinant production of (I); (B) also its oligonucleotide
XX fragments, in standard hybridization and/or amplification assays; (C) as
XX source of antisense molecules or ribozymes; and (D) to produce transgenic
XX animals (for studying (patho)physiology of (I)). Diseases possibly
XX associated with under- or over-expression of (I) are those of the immune,
XX osteogenic, cardiovascular and central or peripheral nervous systems, the
XX tumors, transplant incompatibility, asthma and rheumatoid arthritis. The
XX products of the invention have antitumor, antiasthmatic and
XX antiarthritic activity. This sequence represents the TNF-receptor of the
XX invention.
XX
XX Sequence 300 AA:
SQ
Query Match 100.0%; Score 300; DB 20; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.6e-269;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
OY 1 MRALEPGSLICLVIALPALLPVPVAVRVAETPTYPMDAETGERTLVCACQCPPTGVOR 60
DB 1 MRALEPGSLICLVIALPALLPVPVAVRVAETPTYPMDAETGERTLVCACQCPPTGVOR 60
OY 61 PCRRDSPPTCGCPRRPHYTFQFNWYLERCYCNVLCGEREEERACATNRRACRCRTGTF 120
DB 61 PCRRDSPPTCGCPRRPHYTFQFNWYLERCYCNVLCGEREEERACATNRRACRCRTGTF 120
OY 121 AAAGCTLEHASCPPGAGVIAPCTPSQNTCCQPCPGTFSASSSSSSBOCOPHRNCTALGIA 180
DB 121 AAAGCTLEHASCPPGAGVIAPCTPSQNTCCQPCPGTFSASSSSSSBOCOPHRNCTALGIA 180
OY 181 LNVPPSSSHDTLCTSTGTGFPPLSTRVPGAECERAVIDFAFODISIKRLQRLQALEAPE 240
DB 181 LNVPPSSSHDTLCTSTGTGFPPLSTRVPGAECERAVIDFAFODISIKRLQRLQALEAPE 240
OY 241 GNGPTPRAGRALQIKLRRLTELLGAODGALLVRLQALRVARMGEGRESVREPLVPH 300
DB 241 GNGPTPRAGRALQIKLRRLTELLGAODGALLVRLQALRVARMGEGRESVREPLVPH 300
RESULT 4

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AAV42182
ID AAV42182 standard; protein; 300 AA.
XX
XX AAV42182;
AC
XX
XX 17-DEC-1999 (first entry)
DT
XX
XX Human FLINT #1 protein sequence.
DE
XX
XX Human; FLINT; mFLINT; OP3; tumour necrosis factor receptor; FasL;
XX apoptosis; inflammation; cancer; diabetes; acute liver failure;
XX sepsis; hepatitis; ischaemia-associated injury; hypercoagulation;
XX reperfusion-associated injury; aplastic anaemia; differentiation;
XX growth; myelodysplastic syndrome; pancytopenic condition;
XX myocardial ischaemia.
XX
XX Homo sapiens.
XX
XX WO950413-A2.
XX
XX 07-OCT-1999.
XX
XX 30-MAR-1999; 99WO-US06797.
XX
XX 30-MAR-1998; 98US-0079856.
XX
XX 20-MAY-1998; 98US-0086074.
XX
XX 09-SEP-1998; 98US-0099643.
XX
XX 17-DEC-1998; 98US-0112577.
XX
XX 18-DEC-1998; 98US-0112703.
XX
XX 18-DEC-1998; 98US-0112933.
XX
XX 22-DEC-1998; 98US-0113407.
XX
XX (ELIL ) LILLY & CO ELI.
XX
XX Bumol TF, Dou S, Glasebrook AL, Gould KE, Hale JE, Heuer JG,
XX Hui KY, Kharitonkov A, Mizrahi J, Na S, Nobilit TW, Reidy CA;
XX Song HY, Wang J, Wu X, Zuckerman SH;
XX
XX WPI; 1999-591319/50.
XX N-PSDB; AA225375.
XX
XX Use of mature FLINT for treating acute liver failure, inflammation,
XX cancer, and diabetes - by prevention of Fas-Fas mediated apoptotic
XX and proinflammatory activity
XX
XX Claim 30; Fig 1; 99pp; English.
XX
XX The present invention describes therapeutic applications of mature FLINT
XX (mFLINT) for use in the treatment of acute liver failure. Mature FLINT
XX (mFLINT), which is a member of the tumour necrosis factor receptor
XX superfamily, is used for treating acute liver failure, inflammation of
XX the liver, abnormal hepatocyte apoptosis, sepsis, a disorder associated
XX with inflammation, hepatitis, abnormal apoptosis, an ischaemia-associated
XX injury or disorder such as hypercoagulation (including use with
XX thrombolytic or anti-thrombolytic agents), reperfusion-associated injury
XX or disorder, Type I diabetes, cancer, cell damage or damage to an
XX innocent bystander tissue that is induced by a chemotherapeutic agent or
XX therapeutic irradiation, treating haematopoietic progenitor cells that
XX have been exposed to therapeutic radiation or chemotherapy, aplastic
XX anaemia, myelodysplastic syndrome or a pancytopenic condition. mFLINT is
XX also used for promoting the growth or differentiation of a haematopoietic
XX progenitor cell or CD34+ cell and preventing damage to a cardiac myocyte
XX resulting from abnormal myocardial ischaemia. The present sequence
XX represents human FLINT.
XX
XX Sequence 300 AA:
SQ
Query Match 100.0%; Score 300; DB 20; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.6e-269;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
OY 1 MRALEPGSLICLVIALPALLPVPVAVRVAETPTYPMDAETGERTLVCACQCPPTGVOR 60

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Db      1 MRALEGPGLSLCLVLAIPALLPVPVAVGVAETPTYPWRDAETGERLVCACCPGTGVQR 60
Oy      61 PCRRDSPPTCGPCPRRHHTQFMWNYLERCRVCNVLCGEREEERACHATHNRACRCRTGFF 120
Db      61 PCRRDSPPTCGPCPRRHHTQFMWNYLERCRVCNVLCGEREEERACHATHNRACRCRTGFF 120
Oy      121 AHAGFCLHASCPCPAGVIAETPSQNTQOCPPGTFSASSSSSEOCQPHRNCALTGLA 180
Db      121 AHAGFCLHASCPCPAGVIAETPSQNTQOCPPGTFSASSSSSEOCQPHRNCALTGLA 180
Oy      181 LNVPSSSHDTLCTCTGCTGFPPLSTRVPGAEECEERAVIDVAFODISIKRLQRLQALEAPE 240
Db      181 LNVPSSSHDTLCTCTGCTGFPPLSTRVPGAEECEERAVIDVAFODISIKRLQRLQALEAPE 240
Oy      241 GWGPTPRAGRAALQIKLRRLTELLGADGALLVRLQALRVARMPGLERSVREERFLPVH 300
Db      241 GWGPTPRAGRAALQIKLRRLTELLGADGALLVRLQALRVARMPGLERSVREERFLPVH 300

RESULT 5
AAV17479
ID      AAV17479 standard; Protein: 300 AA.
AC      AAV17479;
DT      02-AUG-1999 (first entry)
DE      Mammalian tumour necrosis factor receptor OPG-2.
XX      Mammalian tumour necrosis factor receptor; OPG-2; Paget's disease;
KM      osteopenic disorder; osteoclast activity; primary osteoporosis;
KW      hyperglycaemia; osteolytic metastasis; immune response; cancer.
OS      Mammalia.
PN      WO926977-A1.
XX      03-JUN-1999.
PD      24-NOV-1998; 98WO-US25065.
XX      17-FEB-1998; 98US-0074896.
PR      24-NOV-1997; 97US-0066446.
XX      (BIOJ ) BIOGEN INC.
PA      (BIOJ ) BIOGEN INC.
PI      Tschopp J;
XX      WPT: 1999-347693/29.
DR      N-PSDB: AAX76052.
XX      New tumour necrosis factor family receptor OPG-2
PT      Claim 1; Page 18; 22pp; English.
XX      PS
XX      The present sequence represents a mammalian tumour necrosis factor
CC      receptor, designated OPG-2. OPG-2, is a member of the tumour necrosis
CC      factor receptor family, and can be used: (i) to raise specific
CC      antibodies (Ab), (ii) to treat osteopenic disorders associated with
CC      excessive osteoclast activity, e.g. primary osteoporosis, Paget's
CC      disease, hyperglycaemia of malignancy, or osteolytic metastases; (iii)
CC      for affinity purification of cognate ligands, and (iv) to screen for
CC      ligands (antagonists or agonists). Ab, or other OPG-2 blocking agents
CC      such as soluble forms of the protein, are used to prevent, or reduce
CC      severity of, an immune response, and for treating cancer. They can also
CC      be used in diagnostic assays. The nucleic acid sequence encoding OPG-2
CC      can be used as a probe to isolate related sequences from other species.
XX      SQ
XX      Sequence 300 AA:
XX      Query Match 100.0%; Score 300; DB 20; Length 300;
XX      Best Local Similarity 100.0%; Pred. No. 1.6e-269;
XX      Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
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```
Oy      1 MRALEGPGLSLCLVLAIPALLPVPVAVGVAETPTYPWRDAETGERLVCACCPGTGVQR 60
Db      1 MRALEGPGLSLCLVLAIPALLPVPVAVGVAETPTYPWRDAETGERLVCACCPGTGVQR 60
Oy      61 PCRRDSPPTCGPCPRRHHTQFMWNYLERCRVCNVLCGEREEERACHATHNRACRCRTGFF 120
Db      61 PCRRDSPPTCGPCPRRHHTQFMWNYLERCRVCNVLCGEREEERACHATHNRACRCRTGFF 120
Oy      121 AHAGFCLHASCPCPAGVIAETPSQNTQOCPPGTFSASSSSSEOCQPHRNCALTGLA 180
Db      121 AHAGFCLHASCPCPAGVIAETPSQNTQOCPPGTFSASSSSSEOCQPHRNCALTGLA 180
Oy      181 LNVPSSSHDTLCTCTGCTGFPPLSTRVPGAEECEERAVIDVAFODISIKRLQRLQALEAPE 240
Db      181 LNVPSSSHDTLCTCTGCTGFPPLSTRVPGAEECEERAVIDVAFODISIKRLQRLQALEAPE 240
Oy      241 GWGPTPRAGRAALQIKLRRLTELLGADGALLVRLQALRVARMPGLERSVREERFLPVH 300
Db      241 GWGPTPRAGRAALQIKLRRLTELLGADGALLVRLQALRVARMPGLERSVREERFLPVH 300

RESULT 6
AAV06817
ID      AAV06817 standard; Protein: 300 AA.
AC      AAV06817;
DT      24-JUN-1999 (first entry)
DE      Human DcR3 polypeptide.
XX      Human DcR3 polypeptide.
KM      DcR3 polypeptide; tumour necrosis factor receptor; TNFR; Fas ligand;
KW      apoptosis; T cell mediated immune response; allergy; asthma; cancer;
KW      rheumatoid arthritis; Crohn's disease; guest vs. host disease; human;
KW      gene therapy.
XX      Homo sapiens.
XX      WO9914330-A1.
XX      25-MAR-1999.
PD      18-SEP-1998; 98WO-US19661.
XX      30-JUL-1998; 98US-0094640.
PR      18-SEP-1997; 97US-0059288.
XX      (GETH ) GENENTECH INC.
PA      Ashkenazi AJ, Bolstein D, Dodge KH, Goddard A, Gurney AJ;
XX      Kim KJ, Lawrence DA, Pittl R, Roy MA, Tumas DB;
XX      Wood WI;
XX      WPT: 1999-244032/20.
DR      N-PSDB: AAX32744.
XX      DcR3 polypeptide related to tumor necrosis factor receptor
XX      Claim 5; Fig 1; 86pp; English.
XX      PS
XX      This represents a human DcR3 polypeptide, a homologue of tumour necrosis
CC      factor receptor (TNFR) polypeptide. Host cells containing a vector
CC      comprising the DcR3 nucleic acid can be used for the recombinant
CC      expression of the protein. DcR3 binds to Fas ligand, so it (or its
CC      chimeras) are useful for modulating apoptosis in mammalian cells, also
CC      other Fas-ligand induced activities, particularly to inhibit T cell
CC      mediated immune responses, e.g. in treatment of allergy, asthma,
CC      rheumatoid arthritis, Crohn's disease, guest vs. host disease etc. DcR3
CC      may also be used to identify specific binding proteins, potential
CC      inhibitors. Antibodies against DcR3 are used to treat cancer,
CC      specifically of the lung and colon, also in diagnosis and for affinity
CC      purification of the protein. Detecting mutations in the gene for DcR3 is
```

CC also used to diagnose cancer, or predisposition to it. DCR3 nucleic acid
 CC is useful as hybridization probe to detect genomic or related sequences;
 CC for chromosome and gene mapping; as source of antisense sequences; for
 CC expression of recombinant DCR3 and to generate transgenic animals (for
 CC development and screening of therapeutic agents), also for in vivo or
 CC ex vivo gene therapy.

XX Sequence 300 AA;

Query Match 100.0%; Score 300; DB 20; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.6e-269;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGGSLTCLVIALPALPVPVAVGVAETPTYPWRDAETGERLVCAQCQPGTFVQR 60
 Db 1 MRALEGGSLTCLVIALPALPVPVAVGVAETPTYPWRDAETGERLVCAQCQPGTFVQR 60
 QY 61 PCRDSPTTCGCPPRHYTGFWMYLERCRVCNVLCGEREEBARACHATNRACRCRTGFF 120
 Db 61 PCRDSPTTCGCPPRHYTGFWMYLERCRVCNVLCGEREEBARACHATNRACRCRTGFF 120
 QY 121 AHAGFCLHASCPPGAGVIAAGTPSONTQCQPCPGTFSSSSSECCQPHRNCTALGTA 180
 Db 121 AHAGFCLHASCPPGAGVIAAGTPSONTQCQPCPGTFSSSSSECCQPHRNCTALGTA 180
 QY 181 LNVPGSSSHDTLCTSCGFPSTRVPGAECERAVIDFVAFODISIKRLQRLQALPAPE 240
 Db 181 LNVPGSSSHDTLCTSCGFPSTRVPGAECERAVIDFVAFODISIKRLQRLQALPAPE 240
 QY 241 GWCPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALRVAMPGLERSVREERFLPVH 300
 Db 241 GWCPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALRVAMPGLERSVREERFLPVH 300

RESULT 7

AAW97749 ID AAW97749 standard; Protein; 300 AA.

XX AAW97749;

XX 21-MAY-1999 (first entry)

XX Human tumour necrosis factor receptor ZTNFR-5.

XX ZTNFR-5; tumour necrosis factor receptor; TNFR; human;

KM cell maturation; bone cell regulation.

XX Homo sapiens.

XX Key Location/Qualifiers

FT Peptide 1..23 /note= "signal peptide"
 FT Protein 24..300 /note= "mature protein"
 FT Domain 24..194 /note= "extracellular domain"
 FT Region 49..71 /note= "cysteine-rich pseudo-repeat 1"
 FT Region 72..113 /note= "cysteine-rich pseudo-repeat 1"
 FT Region 114..151 /note= "cysteine-rich pseudo-repeat 1"
 FT Region 152..194 /note= "cysteine-rich pseudo-repeat 1"
 FT Region /note= "cysteine-rich pseudo-repeat 1"

XX WO9904001-A1.

XX 28-JAN-1999.

XX 21-JUL-1998; 98WO-US15072.

XX 21-JUL-1997; 97US-0053203.

XX

PA (ZYMO) ZYMOGENETICS INC.

XX Farrah TM.

XX WPI: 1999-132245/11.

DR N-PSDB; AAX07226.

PT Novel tumour necrosis factor receptor ZTNFR5 - useful for
 PT regulating maturation of TNF-ligand bearing cells

PS Claim 1; Page 84-85; 109pp; English.

XX This polypeptide comprises a new, secreted tumour necrosis factor
 CC receptor (see AAW97749), designated ZTNFR-5. Novel ZTNFR-5 encoding
 CC polynucleotides and polypeptides were initially identified by
 CC querying an expressed sequence tag (EST) database for sequences
 CC homologous to conserved motifs within the TNF receptor family.
 CC Based on this search, a contig of 16 ESTs (see AAX07226) was
 CC constructed. ZTNFR-5 polypeptides comprise 4 cysteine-rich repeats
 CC (see also AAW9750-55) that are homologous to other TNF receptors, in
 CC particular the soluble, secreted TNF receptor osteoprotegerin.
 CC ZTNFR-5 polypeptide can be prepared by recombinant methods. The
 CC polypeptide, especially the extracellular domain, can be used to
 CC generate a soluble variant of ZTNFR-5. The polypeptides and
 CC nucleic acids can be used to screen for ligands, agonists and
 CC antagonists of ZTNFR-5. The polypeptides can be used in bone cell
 CC regulation and to regulate the maturation of TNF ligand-bearing
 CC cells such as T- or B-cells, lymphocytes, peripheral blood
 CC mononuclear cells, polymorphonuclear leukocytes, fibroblasts or
 CC hematopoietic cells.

XX Sequence 300 AA;

Query Match 100.0%; Score 300; DB 20; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.6e-269;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGGSLTCLVIALPALPVPVAVGVAETPTYPWRDAETGERLVCAQCQPGTFVQR 60
 Db 1 MRALEGGSLTCLVIALPALPVPVAVGVAETPTYPWRDAETGERLVCAQCQPGTFVQR 60
 QY 61 PCRDSPTTCGCPPRHYTGFWMYLERCRVCNVLCGEREEBARACHATNRACRCRTGFF 120
 Db 61 PCRDSPTTCGCPPRHYTGFWMYLERCRVCNVLCGEREEBARACHATNRACRCRTGFF 120
 QY 121 AHAGFCLHASCPPGAGVIAAGTPSONTQCQPCPGTFSSSSSECCQPHRNCTALGTA 180
 Db 121 AHAGFCLHASCPPGAGVIAAGTPSONTQCQPCPGTFSSSSSECCQPHRNCTALGTA 180
 QY 181 LNVPGSSSHDTLCTSCGFPSTRVPGAECERAVIDFVAFODISIKRLQRLQALPAPE 240
 Db 181 LNVPGSSSHDTLCTSCGFPSTRVPGAECERAVIDFVAFODISIKRLQRLQALPAPE 240
 QY 241 GWCPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALRVAMPGLERSVREERFLPVH 300
 Db 241 GWCPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALRVAMPGLERSVREERFLPVH 300

RESULT 8

AAW95082 ID AAW95082 standard; Protein; 300 AA.

XX AAW95082;

XX 20-MAY-1999 (first entry)

XX Orphan receptor (HUMAN NTR-1) polypeptide.

XX HUMAN NTR-1; orphan receptor; osteoprotegerin; OPG; TNFR; human;

KM tumour necrosis factor receptor; muscle disorder; bone mass; screening;
 KM muscle metabolism; binding agent; cognate ligand.

XX Homo sapiens.

XX W09907738-A2.
XX 18-FEB-1999.
XX 04-AUG-1998; 98WO-US16202.
XX 06-AUG-1997; 97US-0054869.
XX (PROC) PROCTER & GAMBLE CO.
XX (RECE-) REGENERON PHARM INC.
XX Maslowski PJ, Morris J, Valenzuela DM;
XX MPI: 1999-167365/14.
XX N-PsDB; AAX22300.
XX
XX Novel orphan human receptor polypeptide and nucleic acid - useful as
XX diagnostic reagents and for treatment of muscle disorders
XX
XX Claim 7; Page 21; 23pp; English.
XX
XX This represents a HUMAN NTR-1 polypeptide, a novel orphan receptor. The
XX protein is related to osteoprotegerin (OPG) and to tumour necrosis factor
XX receptor (TNFR). Host cells transformed with a vector comprising the
XX HUMAN NTR-1 nucleic acid are used for the recombinant expression of the
XX protein. HUMAN NTR-1 proteins and antibodies immuno specific for the
XX protein are useful for diagnosis and treatment of humans and animals,
XX especially muscle disorders, as the receptor is involved in regulation of
XX bone mass and muscle metabolism. HUMAN NTR-1 receptors are also useful
XX for screening for novel binding agents, and cognate ligands, which may be
XX used to treat disorders associated with HUMAN NTR-1 imbalance.
XX
XX Sequence 300 AA:
SQ

Query Match 100.0%; Score 300; DB 20; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.6e-269;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGPGLSLICLVLPALLPVPVAVGVAEPTPTYPMDATGRLVCAOCPPGTFVOR 60
DB 1 MRALEGPGLSLICLVLPALLPVPVAVGVAEPTPTYPMDATGRLVCAOCPPGTFVOR 60
QY 61 PCRRDSPPTCGCPPRHHTQFNNYLERCRYCNVLCGEREEERACHATHNRACRRTGTF 120
DB 61 PCRRDSPPTCGCPPRHHTQFNNYLERCRYCNVLCGEREEERACHATHNRACRRTGTF 120
QY 121 AHAGFCLHASCPPGAGVIAPTGPTSONTOCCPCPGTFSASSSSSEOCQPHNCTALGIA 180
DB 121 AHAGFCLHASCPPGAGVIAPTGPTSONTOCCPCPGTFSASSSSSEOCQPHNCTALGIA 180
QY 181 LNVPGSSSHDITCTGCTGFPPLSTRVPGAEECEERAVIDYFAFDISIKRLQRLQALEAPE 240
DB 181 LNVPGSSSHDITCTGCTGFPPLSTRVPGAEECEERAVIDYFAFDISIKRLQRLQALEAPE 240
QY 241 GWGPPPRAGRAALQKLRRLTELGAODGALLVRLQALRVARMPEGLERSYRERPLPVH 300
DB 241 GWGPPPRAGRAALQKLRRLTELGAODGALLVRLQALRVARMPEGLERSYRERPLPVH 300

RESULT 9
AAB19335
ID AAB19335 standard; Protein; 300 AA.
XX
XX AAB19335;

DT 19-FEB-2001 (first entry)

DE A full length human FAS ligand Inhibitory Protein (FLINT).

XX Human; FAS ligand Inhibitory Protein; FLINT; analogue; apoptosis;
XX tumour necrosis factor receptor; acute lung injury; pulmonary fibrosis;
XX acute respiratory distress syndrome; ulcerative colitis;
KW
KW

KW chronic obstructive pulmonary disease; Crohn's disease.
XX Homo sapiens.
XX W0200058465-A2.
XX
XX 05-OCT-2000.
XX
XX 20-MAR-2000; 2000WO-US06417.
XX
XX 30-MAR-1999; 99US-0126839.
XX 21-JUN-1999; 99US-0140077.
XX 21-JUN-1999; 99US-0140156.
XX 20-OCT-1999; 99US-0160566.
XX 18-FEB-2000; 2000US-0183398.
XX
XX (ELIL) LILLY & CO ELI.
XX
XX Becker GW, Cohen FU, Gonzalez-dewhilt PA, Hale JE, Micnovic R;
XX Newton CM, Noblitt TW, Rathmachalam R, Tschang SR, Witcher DR;
XX Wroblewski VJ;
XX
XX MPI: 2000-656167/63.
XX
XX FAS ligand Inhibitory Protein analogs useful for treating abnormal
XX apoptosis related diseases e.g. acute lung injury, pulmonary fibrosis,
XX chronic obstructive pulmonary disease ulcerative colitis or Crohn's
XX disease
XX
XX Disclosure: Page 113-114; 114pp; English.
XX
XX The present sequence represents a full length human FAS ligand Inhibitory
XX protein (FLINT). FLINT is a homologue of tumour necrosis factor receptor
XX proteins. FLINT inhibits the binding of FAS to FAS ligand. The mature
XX FLINT protein is modified to produce analogues, which have greater
XX potency, longer in vivo half-lives, decreased aggregation, decreased
XX absorption onto surfaces, increased solubility and improved ease of
XX formulation. The FLINT analogue is useful for treating a patient
XX suffering from disease or condition relating to abnormal apoptosis such
XX as acute lung injury, acute respiratory distress syndrome, pulmonary
XX fibrosis, chronic obstructive pulmonary disease, ulcerative colitis, or
XX Crohn's disease.
XX
XX Sequence 300 AA:
SQ

Query Match 100.0%; Score 300; DB 21; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.6e-269;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGPGLSLICLVLPALLPVPVAVGVAEPTPTYPMDATGRLVCAOCPPGTFVOR 60
DB 1 MRALEGPGLSLICLVLPALLPVPVAVGVAEPTPTYPMDATGRLVCAOCPPGTFVOR 60
QY 61 PCRRDSPPTCGCPPRHHTQFNNYLERCRYCNVLCGEREEERACHATHNRACRRTGTF 120
DB 61 PCRRDSPPTCGCPPRHHTQFNNYLERCRYCNVLCGEREEERACHATHNRACRRTGTF 120
QY 121 AHAGFCLHASCPPGAGVIAPTGPTSONTOCCPCPGTFSASSSSSEOCQPHNCTALGIA 180
DB 121 AHAGFCLHASCPPGAGVIAPTGPTSONTOCCPCPGTFSASSSSSEOCQPHNCTALGIA 180
QY 181 LNVPGSSSHDITCTGCTGFPPLSTRVPGAEECEERAVIDYFAFDISIKRLQRLQALEAPE 240
DB 181 LNVPGSSSHDITCTGCTGFPPLSTRVPGAEECEERAVIDYFAFDISIKRLQRLQALEAPE 240
QY 241 GWGPPPRAGRAALQKLRRLTELGAODGALLVRLQALRVARMPEGLERSYRERPLPVH 300
DB 241 GWGPPPRAGRAALQKLRRLTELGAODGALLVRLQALRVARMPEGLERSYRERPLPVH 300

RESULT 10
AAB28559
ID AAB28559 standard; protein; 300 AA.

XX AAB28559;
 AC
 XX
 DF 08-FEB-2001 (first entry)
 DE Human soluble TNF receptor tnfrct-1.
 XX
 KM Human: tumour necrosis factor like-1; TNFL1; tumour necrosis factor; TNF;
 KM immunosuppressive; antiarthritic; neuroprotective; dermatological;
 KM antiinflammatory; antidiabetic; cytostatic; osteopathic; gene therapy;
 KM colon cancer; rheumatoid arthritis; septic shock; Crohn's disease;
 KM osteoporosis; autoimmune disease; myasthenia gravis;
 KM insulin-dependent diabetes mellitus.
 XX
 OS Homo sapiens.
 PN W0200060079-A2.
 PD 12-OCT-2000.
 PF 05-APR-2000; 2000MO-US09058.
 PR 05-APR-1999; 99US-0286529.
 PA (CHIR) CHIRON CORP.
 PI Tribouley C;
 XX WPI; 2000-665004/64.
 DR N-PSDB; AAC63764.
 XX
 PT Tumor necrosis factor (TNF) and TNF receptor superfamily protein
 PT members TNF-L and TNFR-L, useful for enhancing or decreasing TNF
 PT activities such as inducing cell death and lymphoid organogenesis
 PS
 XX Claim 1; Page 72; 77pp; English.
 CC The present sequence is given in a specification relating to an isolated
 CC human protein designated tumour necrosis factor like-1 (TNFL1). It may be
 CC used to induce cell death in tumours, to induce apoptosis of activated T
 CC cells, to induce inflammation, and to rescue resting T cells from
 CC apoptosis. TNF receptors are used to regulate the function of a TNF
 CC ligand which plays a role in apoptosis, inflammation, differentiation, or
 CC proliferation. Expression of the receptors can also be useful as markers
 CC for cancer, especially for colon cancer. Diseases which can be treated
 CC using ligands and/or receptors of the TNF/TNFR superfamily include
 CC rheumatoid arthritis, cancer, septic shock, Crohn's disease and
 CC osteoporosis. The polynucleotides can be used in gene delivery vehicles,
 CC for the purpose of delivering a mRNA or oligonucleotide, full-length
 CC protein, fusion protein, polypeptide, or ribozyme, or single-chain
 CC antibody, into a cell. The newly identified receptor proteins play
 CC regulatory roles in cell proliferation and/or differentiation. The
 CC receptors can also play a role in the negative regulation of
 CC osteoclastogenesis. Soluble TNFR-like receptors can be useful in the
 CC neutralisation of TNF or TNF-like ligands. A TNF-L protein can also be
 CC used to treat autoimmune diseases (myasthenia gravis and
 CC insulin-dependent diabetes mellitus), tumours, and proliferative
 CC disorders. A TNF-L or TNFR-L subgenomic polynucleotide can also be
 CC delivered to subjects for the purpose of screening test compounds for
 CC those which are useful for enhancing transfer of TNF-L subgenomic
 CC polynucleotides to the cell or for enhancing subsequent biological
 CC effects of TNF-L or TNFR-L subgenomic polynucleotides within the cell.
 XX
 SQ Sequence 300 AA;
 Query Match 100.0%; Score 300; DB 21; Length 300;
 Best local similarity 100.0%; Pred. No. 1.6e-269;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 1 MRALBPGSLCLVIALPALLPVPAVRGVAETPTVWRAEGERLYCAQCPEPTVQR 60
 DB 1 MRALBPGSLCLVIALPALLPVPAVRGVAETPTVWRAEGERLYCAQCPEPTVQR 60

QY 61 PCRDSPTTCGCPPRHYTQFMWYLERCRYCNVLGGEREAEARACATNHRACRCRTGFF 120
 DB 61 PCRDSPTTCGCPPRHYTQFMWYLERCRYCNVLGGEREAEARACATNHRACRCRTGFF 120
 QY 121 AAAGFCLERHASCPPGAGVIAVPSPONTQCQPCPPGTFSSSSSECCQHRNCTALGLA 180
 DB 121 AAAGFCLERHASCPPGAGVIAVPSPONTQCQPCPPGTFSSSSSECCQHRNCTALGLA 180
 QY 181 LNPSSSHHTLCTSCGFPFLSTRVPGAECECAVIDFAFODISTIKRLQALQALEAPE 240
 DB 181 LNPSSSHHTLCTSCGFPFLSTRVPGAECECAVIDFAFODISTIKRLQALQALEAPE 240
 QY 241 GMGPTPRAGAAALQKLRRLTELLGAODGALLVRLDIALRVARMGLESVEREFLPVH 300
 DB 241 GMGPTPRAGAAALQKLRRLTELLGAODGALLVRLDIALRVARMGLESVEREFLPVH 300
 RESULT 11
 AAB24057
 ID AAB24057 standard; Protein; 300 AA.
 AC AAB24057;
 XX
 DT 29-JAN-2001 (first entry)
 XX
 DE Human PRO212 protein sequence SEQ ID NO:2.
 XX
 KM Human; tumour; diagnosis; neoplastic disease; neoplastic cell growth;
 KM proliferation; tumorigenesis; identification; cancer; cytostatic;
 KM neurotropic; neuroprotective; antiinflammatory; immunosuppressive;
 KM immunostimulant; antiangiogenic; leukaemia; lymphoid malignancy;
 KM neuronal disorder; glial disorder; astrocytal disorder; angiogenic;
 KM hypothalamic disorder; glandular disorder; macrophagal disorder;
 KM epithelial disorder; stromal disorder; blastocytic disorder;
 KM inflammatory disorder; immunologic disorder.
 XX
 OS Homo sapiens.
 PN W0200053755-A2.
 PD 14-SEP-2000.
 PF 06-JAN-2000; 2000MO-US00376.
 PR 08-MAR-1999; 99MO-US05028.
 PR 02-JUN-1999; 99MO-US12252.
 PR 23-JUN-1999; 99US-0141037.
 PR 07-JUL-1999; 99US-0143048.
 PR 26-JUL-1999; 99US-0145698.
 PR 30-NOV-1999; 99MO-US28313.
 PR 20-DEC-1999; 99MO-US30911.
 PR 03-JAN-2000; 2000MO-US00219.
 PA (GETH) GENENTECH INC.
 PI Ashkenazi AJ, Baker KP, Goddard A, Gurney AL, Hillan KJ, Roy MA;
 PI Watanabe CK, Wood WI;
 PI WPI; 2000-572270/53.
 DR N-PSDB; AAC58367.
 XX
 PT Thirty PRO polynucleotides encoding PRO polypeptides, useful in the
 PT treatment, diagnosis and prevention of cancer -
 PS
 XX Claim 61; Fig 2; 286pp; English.
 XX
 CC The present invention describes an isolated antibody that binds to
 CC one of the human PRO proteins designated PRO212, PRO290, PRO341, PRO355,
 CC PRO619, PRO717, PRO809, PRO830, PRO848, PRO943, PRO1005, PRO1009,
 CC PRO1025, PRO1030, PRO1097, PRO1107, PRO1111, PRO1153, PRO1182, PRO1184,
 CC PRO1187, PRO1281, PRO39, PRO834, PRO1317, PRO1710, PRO2094,
 CC PRO2145 OR PRO2198. PRO antagonists can be used to inhibit tumour cell
 CC growth. The PRO polypeptides and nucleotides are useful in the

CC treatment, diagnosis and prevention of cancer. The antibodies and other
 CC anti-tumour compounds maybe used to treat various conditions, including
 CC those characterised by overexpression and/or activation of the amplified
 CC PRO genes. Exemplary conditions or disorders to be treated with such
 CC antibodies and other compounds include benign or malignant tumours.
 CC (e.g., renal, liver, kidney, bladder, breast, gastric, ovarian,
 CC colorectal, prostate, pancreatic, lung, vulva, thyroid, hepatic
 CC carcinomas, sarcomas, glioblastomas, and various head and neck tumours),
 CC leukaemias and lymphoid malignancies, other disorders such as neuronal,
 CC gliol, astrocytal, hypohalamic and other glandular, macrophagal,
 CC epithelial, stromal and blastocoele disorders, and inflammatory,
 CC angiogenic and immunologic disorders. AAC58242 to AAC58366 represent PCR
 CC primers and hybridisation probes used in the isolation of the human PRO
 CC sequences. AAC58367 to AAC58396 and AAB24057 to AAB24089 represent human
 CC PRO polynucleotide and protein sequences given in the exemplification of
 CC the present invention.

XX
 SQ Sequence 300 AA;

Query Match 100.0%; Score 300; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.6e-269;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 MRALEBPGSLSLCLVIALPAPVAVRVAETPTPTWDAETGERLVCAQCPPTFVOR 60
 DB 1 MRALEBPGSLSLCLVIALPAPVAVRVAETPTPTWDAETGERLVCAQCPPTFVOR 60
 OY 61 PRRBDSPTTCGPPPHRYTQFMNNYLERCYCNVLCGEREERARACATNRCRCRTGFF 120
 DB 61 PRRBDSPTTCGPPPHRYTQFMNNYLERCYCNVLCGEREERARACATNRCRCRTGFF 120
 OY 121 AAAGFCLERHASCPPGAGVIAPTGPTSONTCQCPPTGFSASSSSSSBQCPHNRCTALGIA 180
 DB 121 AAAGFCLERHASCPPGAGVIAPTGPTSONTCQCPPTGFSASSSSSSBQCPHNRCTALGIA 180
 OY 181 LNVPGSSSHDTLCTSTGTGFPPLSTRVPGAECERAVYDFAFQDISKRLRLQALEAPE 240
 DB 181 LNVPGSSSHDTLCTSTGTGFPPLSTRVPGAECERAVYDFAFQDISKRLRLQALEAPE 240
 OY 241 GNGPFRAGRAALQKLRRLTELLGAQDALLVRLQALRVARMPGLERSYRERPLPVH 300
 DB 241 GNGPFRAGRAALQKLRRLTELLGAQDALLVRLQALRVARMPGLERSYRERPLPVH 300

RESULT 12
 AAB33416
 ID AAB33416 standard; Protein; 300 AA.
 XX AAB33416;
 AC
 XX
 XX 29-JAN-2001 (first entry)
 DT
 XX
 XX Human PRO212 protein UNQ186 SEQ ID NO:14.
 DE
 XX
 XX Human; immune related disease; diagnosis; antiinflammatory; cardiant;
 KW dermatological; antiarthritic; antirheumatic; immunosuppressive;
 KW haemostatic; antidiabetic; antidiabetic; neoprotective;
 KW antianemic; hepatotropic; virucide; antiprotic; antiallergic;
 KW antistatic; systemic lupus erythematosus; rheumatoid arthritis;
 KW osteoarthritis; spondyloarthropathy; systemic sclerosis; sarcoidosis;
 KW idiopathic inflammatory myopathy; Sjogren's syndrome; thyroiditis;
 KW systemic vasculitis; autoimmune haemolytic anaemia; diabetes mellitus;
 KW autoimmune thrombocytopenia; immune-mediated renal disease;
 KW demyelinating disease; hepatobiliary disease; Whipple's disease;
 KW inflammatory bowel disease; gluten-sensitive enteropathy;
 KW autoimmune disease; immune-mediated skin disease; allergic disease;
 KW immunological disease; transplantation associated disease;
 KW graft rejection; graft-versus-host-disease.
 XX
 OS Homo sapiens.
 XX
 PN WO200053758-A2.
 XX

PD 14-SEP-2000.
 XX
 PF 02-MAR-2000; 2000MO-US05841.
 XX
 PR 08-MAR-1999; 99MO-US05028.
 PR 10-MAR-1999; 99US-0123618.
 PR 12-MAR-1999; 99US-0123957.
 PR 23-MAR-1999; 99US-0125775.
 PR 12-APR-1999; 99US-0128849.
 PR 20-APR-1999; 99MO-US08615.
 PR 28-APR-1999; 99US-0131445.
 PR 04-MAY-1999; 99US-0132371.
 PR 14-MAY-1999; 99US-0134287.
 PR 02-JUN-1999; 99MO-US12252.
 PR 23-JUN-1999; 99US-0141037.
 PR 26-JUL-1999; 99US-0144758.
 PR 26-JUL-1999; 99US-0145698.
 PR 28-JUL-1999; 99US-0146222.
 PR 01-SEP-1999; 99MO-US20111.
 PR 08-SEP-1999; 99MO-US20594.
 PR 13-SEP-1999; 99MO-US20944.
 PR 15-SEP-1999; 99MO-US21090.
 PR 15-SEP-1999; 99MO-US21547.
 PR 05-OCT-1999; 99MO-US23089.
 PR 29-OCT-1999; 99US-0162506.
 PR 29-NOV-1999; 99MO-US28214.
 PR 30-NOV-1999; 99MO-US28313.
 PR 30-NOV-1999; 99MO-US28409.
 PR 01-DEC-1999; 99MO-US28301.
 PR 01-DEC-1999; 99MO-US28634.
 PR 02-DEC-1999; 99MO-US28551.
 PR 02-DEC-1999; 99MO-US28564.
 PR 16-DEC-1999; 99MO-US30095.
 PR 20-DEC-1999; 99MO-US30999.
 PR 30-DEC-1999; 99MO-US31274.
 PR 05-JAN-2000; 2000MO-US00219.
 PR 06-JAN-2000; 2000MO-US00377.
 PR 11-FEB-2000; 2000MO-US03565.
 PR 18-FEB-2000; 2000MO-US04341.
 PR 18-FEB-2000; 2000MO-US04342.
 PR 22-FEB-2000; 2000MO-US04414.
 XX
 XX (GETH) GENENTECH INC.
 PA
 XX Ashkenazi AJ, Baker KP, Goddard A, Gurney AL, Hebert C, Henzel W;
 PI Kabakoff RC, Lu Y, Pan J, Pennica D, Shelton DL, Smith V;
 PI Stewart TA, Tumas D, Watanabe CK, Wood WI, Yan M;
 XX
 DR WPI; 2000-572271/53.
 DR N-PSDB; AAC58581.
 XX
 PT Sixty four PRO polypeptides, useful in the diagnosis and treatment of
 PT immune related disorders, e.g. systemic lupus erythematosus, rheumatoid
 PT arthritis, osteoarthritis, thyroiditis and diabetes mellitus -
 PS
 XX Claim 33; Fig 6; 309pp; English.

XX The present invention describes sixty four human PRO proteins which can
 CC be used in the treatment of immune related diseases. The human PRO
 CC proteins, anti-PRO antibodies, agonists and antagonists are useful for
 CC treating and diagnosing immune related disorders. The disorders are
 CC selected from systemic lupus erythematosus, rheumatoid arthritis,
 CC osteoarthritis, juvenile chronic arthritis, spondyloarthropathies,
 CC systemic sclerosis, idiopathic inflammatory myopathies, Sjogren's
 CC syndrome, systemic vasculitis, sarcoidosis, autoimmune haemolytic
 CC anaemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus,
 CC immune-mediated renal disease, demyelinating diseases of the central
 CC and peripheral nervous systems, hepatobiliary diseases, inflammatory
 CC bowel disease, gluten-sensitive enteropathy and Whipple's disease,
 CC autoimmune or immune-mediated skin diseases, allergic diseases,
 CC immunological diseases of the lung, and transplantation associated

CC diseases including graft rejection and graft-versus-host-disease.
 CC AAC58397 to AAC58578 represent PCR primers and hybridisation probes used
 CC in the isolation of human PRO sequences. AAC58579 to AAC58642 and
 CC AAB33414 to AAB33477 represent human PRO polynucleotide and protein
 CC sequences given in the exemplification of the present invention.

XX Sequence 300 AA;

Query Match 100.0%; Score 300; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.6e-269; Indels 0; Gaps 0;
 Matches 300; Conservative 0; Mismatches 0;

QY 1 MRALEGGSLICLVLPALPYPVAVGVAETPTYPWDAETGERLYCACCPGTFYQR 60
 DB 1 MRALEGGSLICLVLPALPYPVAVGVAETPTYPWDAETGERLYCACCPGTFYQR 60
 QY 61 PCRRDSPPTGCPGPPRHHTQFWNYLERCRVNVLCGEREBARACHATHNRCRCRTGFF 120
 DB 61 PCRRDSPPTGCPGPPRHHTQFWNYLERCRVNVLCGEREBARACHATHNRCRCRTGFF 120
 QY 121 AHAGFCLFHASCPCGAGVIAGTPSONTCQPCPGPTFSASSSSSECCQPHRNTAGLA 180
 DB 121 AHAGFCLFHASCPCGAGVIAGTPSONTCQPCPGPTFSASSSSSECCQPHRNTAGLA 180
 QY 181 LNVGSSSHDTLCTSGTGFPLSTRVPGAEECEERAVIDFVAFODISIKRLQRLQALEAPE 240
 DB 181 LNVGSSSHDTLCTSGTGFPLSTRVPGAEECEERAVIDFVAFODISIKRLQRLQALEAPE 240
 QY 241 GMSGPTPRAGRAALQKLRRLTELLGAODGALLVRLQALVAVAMPGLERSVRRFLPVH 300
 DB 241 GMSGPTPRAGRAALQKLRRLTELLGAODGALLVRLQALVAVAMPGLERSVRRFLPVH 300

RESULT 13

AAB03621 standard; Protein; 300 AA.

AC AAB03621;

DT 03-JAN-2001 (first entry)

XX Human Fas ligand inhibitor FLINT.

KW Human; Fas ligand inhibitor; FLINT; apoptosis; autoimmune disease;

KW inflammation; infectious disease; ischaemia; Alzheimer's disease;

KW Parkinson's disease; Crohn's disease; transplantation.

XX Homo sapiens.

XX Key Location/Qualifiers

FT Peptide 1..29 /label= signal_peptide

FT Protein 30..300 /label= mature_FLINT

FT Domain 1..42 /label= domain_1

FT Domain 43..85 /label= domain_2

FT Domain 86..122 /label= domain_3

FT Domain 123..165 /label= domain_4

XX MO200034782-A1.

XX 15-JUN-2000.

XX 07-DEC-1999; 99WO-US28696.

XX 09-DEC-1998; 98US-0111575.

XX 09-DEC-1998; 98US-0111580.

XX 07-JAN-1999; 99US-0115069.

PA (ELIL) LILLY & CO ELI.

XX Rostock PRJ, Song HY, Su EW;

XX WPI; 2000-431379/37.

DR N-PSDB; AAA53208.

XX Novel monkey Fas ligand inhibitor polypeptides, useful for treating

PT inflammatory or autoimmune disease such as rheumatoid arthritis,

PT infectious diseases such as chronic hepatitis, and

PT ischaemia/Re-perfusion conditions -

XX Claim 19; Page 91-93; 101pp; English.

CC The present sequence is the protein sequence of the human Fas ligand
 CC inhibitor (FLINT). The FLINT protein is involved in cell-specific
 CC apoptosis, and can be used to treat inflammatory and autoimmune diseases
 CC such as rheumatoid arthritis, inflammatory bowel disease,
 CC graft-versus-host disease, diabetes, psoriasis and Graves' disease,
 CC infectious diseases such as HIV-induced lymphopenia, fulminant viral
 CC hepatitis B/C, chronic hepatitis and cirrhosis, and H. pylori-associated
 CC ulceration, ischaemia and reperfusion conditions including acute failure
 CC myocardial infarction, acute coronary syndrome, congestive heart failure
 CC and atherosclerosis, and Alzheimer's and Parkinson's diseases, acute lung
 CC injury and acute respiratory distress syndrome, Crohn's disease, brain
 CC trauma and injury, chronic glomerulonephritis, osteoporosis, aplastic
 CC anaemia, myelodysplasia, ulcerative colitis, Down's syndrome, and
 CC multiple sclerosis. In addition, the protein and its gene can be used to
 CC prevent apoptosis following organ transplantation.

XX Sequence 300 AA;

Query Match 100.0%; Score 300; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.6e-269; Indels 0; Gaps 0;
 Matches 300; Conservative 0; Mismatches 0;

QY 1 MRALEGGSLICLVLPALPYPVAVGVAETPTYPWDAETGERLYCACCPGTFYQR 60

DB 1 MRALEGGSLICLVLPALPYPVAVGVAETPTYPWDAETGERLYCACCPGTFYQR 60

QY 61 PCRRDSPPTGCPGPPRHHTQFWNYLERCRVNVLCGEREBARACHATHNRCRCRTGFF 120

DB 61 PCRRDSPPTGCPGPPRHHTQFWNYLERCRVNVLCGEREBARACHATHNRCRCRTGFF 120

QY 121 AHAGFCLFHASCPCGAGVIAGTPSONTCQPCPGPTFSASSSSSECCQPHRNTAGLA 180

DB 121 AHAGFCLFHASCPCGAGVIAGTPSONTCQPCPGPTFSASSSSSECCQPHRNTAGLA 180

QY 181 LNVGSSSHDTLCTSGTGFPLSTRVPGAEECEERAVIDFVAFODISIKRLQRLQALEAPE 240

DB 181 LNVGSSSHDTLCTSGTGFPLSTRVPGAEECEERAVIDFVAFODISIKRLQRLQALEAPE 240

QY 241 GMSGPTPRAGRAALQKLRRLTELLGAODGALLVRLQALVAVAMPGLERSVRRFLPVH 300

DB 241 GMSGPTPRAGRAALQKLRRLTELLGAODGALLVRLQALVAVAMPGLERSVRRFLPVH 300

RESULT 14

AAV97246 standard; Protein; 300 AA.

AC AAV97246;

DT 19-DEC-2000 (first entry)

XX M68 TNF receptor related protein.

KW M68; tumour necrosis factor; TNF; programmed cell death; apoptosis;

KW receptor; immune response; cell differentiation; ligand; cancer;

KW bone disease; systemic lupus erythematosus; Hashimoto's thyroiditis;

KW Grave's disease; idiopathic myxedema; autoimmune diabetes;

KW thrombotic thrombocytopenic purpura; multiple sclerosis;

KW liver diseases; autoimmune gastritis; ulcerative colitis;

KW glomerulonephritis; pulmonary fibrosis; heart failure;
 KW atherosclerosis; aplastic anaemia; myelodysplastic syndromes;
 KW osteoporosis; Alzheimers disease; Parkinsons disease; stroke;
 KW myocardial infarction; human.
 OS Homo sapiens.
 XX MO200046247-A1.
 XX 10-AUG-2000.
 XX
 XX 04-FEB-2000; 2000WO-US03037.
 XX
 XX 05-FEB-1999; 99US-0118902.
 XX 20-DEC-1999; 99US-0172754.
 XX
 XX (MERI) MERCK & CO INC.
 XX Bal C;
 XX WPI: 2000-506066/45.
 DR N-PSDB: AAA53800, AAA53801, AAA53802.
 XX
 PT Isolated human M68 nucleic acids and proteins which are part of the
 PT tumor necrosis factor receptor (TNFR) family, useful for identifying
 PT osteoporosis, Alzheimer's disease
 XX
 PS Claim 1; Page 75-76; 80pp; English.
 XX
 CC The M68 protein is a member of a family of proteins which have
 CC roles in immune responses, cell death, cell proliferation and
 CC stimulation of cell differentiation. M68 lacks a transmembrane domain
 CC and is a secreted factor suggesting that it functions as a natural
 CC inhibitor for its ligand. The altered expression pattern of M68 in a
 CC multitude of tissues suggests that M68 may play a role in cancer by
 CC binding to its ligand and blocking apoptotic cell death induced by
 CC such a ligand. This anti-apoptotic role of M68 suggests that
 CC modulators of M68 will be useful in treatment of apoptosis-related
 CC diseases such as various forms of cancer and various bone disorders.
 CC M68 nucleic acids and proteins are therefore useful for treating
 CC conditions involving atypical apoptosis and for identifying
 CC modulators of M68. Modulators of M68 are useful for treatment of
 CC cancer and other diseases associated with abnormal levels of
 CC apoptosis including systemic lupus erythematosus, Hashimoto's
 CC thyroiditis, Grave's disease, idiopathic myxedema, autoimmune
 CC diabetes, thrombotic thrombocytopenic purpura, multiple sclerosis,
 CC liver diseases, autoimmune gastritis, ulcerative colitis,
 CC glomerulonephritis, pulmonary fibrosis, heart failure,
 CC atherosclerosis, aplastic anaemia, myelodysplastic syndromes,
 CC osteoporosis, Alzheimers disease, Parkinsons disease, stroke, and
 CC myocardial infarction.
 XX
 SQ Sequence 300 AA;
 Query Match 100.0%; Score 300; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.6e-269;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 Oy 1 MRALLEGSLTLCVLTALPPLPVAAGVAEPTTYPWRAETGERIVCAQCPPTGVOR 60
 Db 1 MRALLEGSLTLCVLTALPPLPVAAGVAEPTTYPWRAETGERIVCAQCPPTGVOR 60
 Oy 61 PCRDSPTTCGPPRRHYTOFWNVLERCRCNVLCGRREBARCATTHNRACCRITGFF 120
 Db 61 PCRDSPTTCGPPRRHYTOFWNVLERCRCNVLCGRREBARCATTHNRACCRITGFF 120
 Oy 121 AAAGFLEHASCPGAGVIAPTGPPSQTQOCPCPGTFSASSSSSECCQPHRNCATGLA 180
 Db 121 AAAGFLEHASCPGAGVIAPTGPPSQTQOCPCPGTFSASSSSSECCQPHRNCATGLA 180
 Oy 181 LNPFGSSHDLTCTSCGFLSTRVPAECCERAVIDFVAFODISTIRLQRLQALEAPE 240
 Db 181 LNPFGSSHDLTCTSCGFLSTRVPAECCERAVIDFVAFODISTIRLQRLQALEAPE 240

Db 181 LNPFGSSHDLTCTSCGFLSTRVPAECCERAVIDFVAFODISTIRLQRLQALEAPE 240
 Oy 241 GWCPTPRAGRAALQKLRRLTELLGADGALLVRLQALVARPMPLERSVEREPLPVH 300
 Db 241 GWCPTPRAGRAALQKLRRLTELLGADGALLVRLQALVARPMPLERSVEREPLPVH 300
 RESULT 15
 ID AAY90357 standard; Protein: 300 AA.
 XX
 XX AAY90357;
 XX
 XX 04-DEC-2000 (first entry)
 XX
 DE Human tumour necrosis factor receptor-6 alpha protein sequence.
 XX
 KW Human; Tumour necrosis factor receptor 6; TNFR-6alpha; TNFR-6beta;
 KW ocular neovascularisation; solid tumour; malignancy; prostate cancer;
 KW breast cancer; colon cancer; diabetic retinopathy; microbial infection;
 KW pre-maturity macular degeneration; allergy; inflammation; tissue damage;
 KW thyroid associated ophthalmopathy; cell damage; parasitic infection;
 KW bone disease; osteoporosis; atherosclerosis; cardiovascular disease;
 KW neurodegenerative disorder; Alzheimer's disease; immune disorder;
 KW graft rejection; rheumatism; liver disease; autoimmune diabetes; asthma;
 KW psoriasis; septic shock; ulcerative colitis; therapy.
 XX
 OS Homo sapiens.
 XX
 XX WO200052028-A1.
 XX
 XX 08-SEP-2000.
 XX
 XX 03-MAR-2000; 2000WO-US05686.
 XX
 XX 04-MAR-1999; 99US-0121774.
 XX 12-MAR-1999; 99US-0124092.
 XX 27-APR-1999; 99US-0131279.
 XX 30-APR-1999; 99US-0131964.
 XX 02-AUG-1999; 99US-0146371.
 XX 01-DEC-1999; 99US-0168235.
 XX
 XX (HUMA-) HUMAN GENOME SCI INC.
 XX
 XX Gentz RL, Ni J, Ebner R, Yu G, Ruben SM, Feng P;
 WPI: 2000-572174/53.
 N-PSDB: AAA37772.
 PT Nucleic acids encoding human tumour necrosis factor receptor (TNFR)
 PT proteins TNFR-6alpha and TNFR-6beta, useful for treating e.g.
 PT Alzheimer's disease, osteoporosis and graft rejection
 XX
 PS Claim 20; Fig 1; 332pp; English.
 XX
 XX This sequence represents the human tumour necrosis factor receptor 6
 XX alpha (TNFR-6alpha) of the invention. The TNFR-6alpha and TNFR-6beta
 XX and protein sequences can be used in the prevention, treatment and
 XX diagnosis of diseases associated with inappropriate TNFR expression. The
 XX nucleic acids, polypeptides, antibodies, agonists and antagonists against
 XX them may be used for the treatment of a range of conditions such as
 XX disorders associated with neovascularisation (especially ocular
 XX neovascularisation) (such as solid tumours and malignancies (e.g.
 XX prostate cancer, breast cancer and colon cancer), diabetic retinopathy
 XX and pre-maturity macular degeneration), allergies, inflammation,
 XX thyroid associated ophthalmopathy, tissue/cell damage, wounds, microbial
 XX and parasitic infections, bone disease (e.g. osteoporosis),
 XX atherosclerosis, pain, cardiovascular disease (e.g. stroke),
 XX neurodegenerative disorders (e.g. Alzheimer's disease), immune
 XX disorders (e.g. graft rejection), rheumatism, liver disease,
 XX autoimmune diabetes, asthma, psoriasis, septic shock and ulcerative
 XX colitis.

SQ Sequence 300 AA;

Query Match 100.0%; Score 300; DB 21; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.6e-269;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
QY 1 MRALEGFGLSLCLVIALPALPVPVAVGVAETPTYPWRDAETGERLVCAQCPGTFVQR 60
    |||
Db 1 MRALEGFGLSLCLVIALPALPVPVAVGVAETPTYPWRDAETGERLVCAQCPGTFVQR 60
    |||
QY 61 PCRDSPTTGGPCPPRHYYTOFWNYLERRCYCNVLCGEREBARACHATNHRACRRTGFF 120
    |||
Db 61 PCRDSPTTGGPCPPRHYYTOFWNYLERRCYCNVLCGEREBARACHATNHRACRRTGFF 120
    |||
QY 121 AHAGFCLEHASCPGAGVIAAGTPSONTOGCPGPGTFSSSSSECCOPHRNCTALGLA 180
    |||
Db 121 AHAGFCLEHASCPGAGVIAAGTPSONTOGCPGPGTFSSSSSECCOPHRNCTALGLA 180
    |||
QY 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECECERAVIDFVAFODISIKRLQRLQALEAPE 240
    |||
Db 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECECERAVIDFVAFODISIKRLQRLQALEAPE 240
    |||
QY 241 GMGPTPRAGRAALQLKLRRLTELLGAQDGALLVRLQLALRVAMPGLERSVREERFLPVH 300
    |||
Db 241 GMGPTPRAGRAALQLKLRRLTELLGAQDGALLVRLQLALRVAMPGLERSVREERFLPVH 300
    |||
```

Search completed: July 16, 2003, 19:40:30
Job time : 39 secs

GenCore version 5.1.6
Copyright (c) 1993 - 2003 CompuGen Ltd.

OM protein - protein search, using sw model

Run on: July 16, 2003, 19:37:34 ; Search time 11 Seconds

(without alignments)

1131.173 Million cell updates/sec

Title: US-09-935-727-2

Perfect score: 300

Sequence: 1 MRALSGPGSLSLCLVIALPA.....RVARMGRLSRVREPLPVH 300

Scoring table: OLIGO

Gapop 60.0 , Gapext 60.0

Searched: 112892 seqs, 41476328 residues

Word size : 0

Total number of hits satisfying chosen parameters: 112892

Minimum DB seq length: 0

Maximum DB seq length: 200000000

Post-processing: Listing first 45 summaries

Database : SwissProt_40.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | Query Match | Length | ID | Description |
|------------|-------|-------------|--------|--------------|---------------------|
| 1 | 300 | 100.0 | 300 | 1 TR6B_HUMAN | 095407 homo sapien |
| 2 | 9 | 3.0 | 430 | 1 TR6B_HUMAN | 096924 homo sapien |
| 3 | 9 | 3.0 | 430 | 1 TR6B_HUMAN | 090922 macaca fasc |
| 4 | 8 | 2.7 | 130 | 1 OREX_CANFA | 090166 canis faml |
| 5 | 8 | 2.7 | 130 | 1 OREX_MOUSE | 055241 mus musculu |
| 6 | 8 | 2.7 | 130 | 1 OREX_MOUSE | 055232 rattus norv |
| 7 | 8 | 2.7 | 131 | 1 OREX_HUMAN | 043612 homo sapien |
| 8 | 8 | 2.7 | 131 | 1 OREX_HUMAN | 077668 sus scrofa |
| 9 | 8 | 2.7 | 179 | 1 CAS2_RAT | 002862 mus musculu |
| 10 | 8 | 2.7 | 184 | 1 CAS2_MOUSE | 061578 mus musculu |
| 11 | 8 | 2.7 | 494 | 1 ADRO_MOUSE | 077432 escherichia |
| 12 | 8 | 2.7 | 530 | 1 YDEV_ECOLI | 068280 n glucosam |
| 13 | 8 | 2.7 | 626 | 1 GLMS_NOS9 | 035442 homo sapien |
| 14 | 8 | 2.7 | 1172 | 1 TSP2_HUMAN | 009910 canis faml |
| 15 | 7 | 2.3 | 27 | 1 SECR_CANFA | 032647 cryotolagus |
| 16 | 7 | 2.3 | 27 | 1 SECR_RABIT | 031299 ovis aries |
| 17 | 7 | 2.3 | 27 | 1 SECR_SHEEP | 076201 phoneutria |
| 18 | 7 | 2.3 | 82 | 1 TX32_PHONI | 033637 escherichia |
| 19 | 7 | 2.3 | 113 | 1 IMMO_ECOLI | 020985 escherichia |
| 20 | 7 | 2.3 | 113 | 1 IMMO_ECOLI | 022558 shigella so |
| 21 | 7 | 2.3 | 113 | 1 IMMO_SHISO | 034628 caenorhabdi |
| 22 | 7 | 2.3 | 114 | 1 YOJ5_CABEL | 025316 azospirillum |
| 23 | 7 | 2.3 | 118 | 1 YNIF_AZOB | 009663 homo sapien |
| 24 | 7 | 2.3 | 121 | 1 SECR_MOUSE | 008535 mus musculu |
| 25 | 7 | 2.3 | 131 | 1 SECR_MOUSE | 008535 mus musculu |
| 26 | 7 | 2.3 | 133 | 1 SECR_MOUSE | 008535 mus musculu |
| 27 | 7 | 2.3 | 134 | 1 SECR_MOUSE | 008535 mus musculu |
| 28 | 7 | 2.3 | 145 | 1 TASM_BFDV | 031895 budgerigar |
| 29 | 7 | 2.3 | 198 | 1 AMOS_DROME | 039087 drosophila |
| 30 | 7 | 2.3 | 198 | 1 TH13_TFAST | 038826 saccharomyc |
| 31 | 7 | 2.3 | 208 | 1 PYRE_PYRAB | 090225 pyrococcus |
| 32 | 7 | 2.3 | 208 | 1 PYRE_PYRHO | 058462 pyrococcus |
| 33 | 7 | 2.3 | 211 | 1 PYRE_PYRFU | 080411 pyrococcus |

ALIGNMENTS

| RESULT 1 | ID | TR6B_HUMAN | STANDARD | PRT | 300 AA. |
|----------|---|------------|----------|-----|---------|
| AC | 095407 | | | | |
| DT | 15-JUN-2002 (Rel. 41, Created) | | | | |
| DT | 15-JUN-2002 (Rel. 41, Last sequence update) | | | | |
| DE | Tumor necrosis factor receptor superfamily member 6B precursor (Decoy receptor for Fas ligand) (Decoy receptor 3) (DCR3) (M68). | | | | |
| GN | TNFRSF6B OR DCR3 OR TR6. | | | | |
| OS | Homo sapiens (Human). | | | | |
| OC | Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; | | | | |
| OC | Mammalia; Eutheria; Primates; Catarrhini; Homiidae; Homo. | | | | |
| OX | NCBI_TaxID=9606. | | | | |
| RN | [1] | | | | |
| RP | SEQUENCE FROM N.A. | | | | |
| RC | TISSUE=Fetal lung; | | | | |
| RX | MEDLINE=99087326; PubMed=9872321; | | | | |
| RA | Pitt R.M., Marsters S.A., Lawrence D.A., Roy M., Kischkel F.C., | | | | |
| RA | Dowd P., Huang A., Donahue C.J., Sherwood S.W., Baldwin D.T., | | | | |
| RA | Godowski P.J., Wood W.I., Gurney A.L., Hillan K.J., Cohen R.L., | | | | |
| RA | Godard A.D., Holstein D., Ashkenazi A.; | | | | |
| RT | "A newly identified member of tumor necrosis factor receptor superfamily (TR6) suppresses LIGHT-mediated apoptosis."; | | | | |
| RL | J. Biol. Chem. 274:13733-13736(1999). | | | | |
| RN | [2] | | | | |
| RP | SEQUENCE FROM N.A., AND SEQUENCE OF 30-35. | | | | |
| RC | TISSUE=Prostate; | | | | |
| RX | MEDLINE=99253915; PubMed=10318773; | | | | |
| RA | Yu K.-Y., Kwon B., Ni J., Zhai Y., Ebner R., Kwon B.S.; | | | | |
| RA | "A newly identified member of tumor necrosis factor receptor superfamily (TR6) suppresses LIGHT-mediated apoptosis."; | | | | |
| RL | J. Biol. Chem. 274:13733-13736(1999). | | | | |
| RN | [3] | | | | |
| RP | SEQUENCE FROM N.A. | | | | |
| RC | TISSUE=Lung; | | | | |
| RX | MEDLINE=20122600; PubMed=10655513; | | | | |
| RA | Bai C., Connolly B., Metzger M.L., Hilliard C.A., Liu X., Sandig V., | | | | |
| RA | Soderman A., Galloway S.M., Liu Q., Austin C.P., Caskey C.T.; | | | | |
| RT | "Overexpression of M66/DCR3 in human gastrointestinal tract tumors independent of gene amplification and its location in a four-gene cluster."; | | | | |
| RL | Proc. Natl. Acad. Sci. U.S.A. 97:1230-1235(2000). | | | | |
| RN | [4] | | | | |
| RP | SEQUENCE FROM N.A. | | | | |
| RA | Matthews L.; | | | | |
| RL | Submitted (NOV-2000) to the EMBL/GenBank/DBJ databases. | | | | |
| RN | [5] | | | | |
| RP | SEQUENCE FROM N.A. | | | | |
| RC | TISSUE=Lung; | | | | |
| RA | Strausberg R.; | | | | |
| RL | Submitted (NOV-2001) to the EMBL/GenBank/DBJ databases. | | | | |
| CC | - FUNCTION: Decoy receptor for the cytotoxic ligands TNFSF14/LIGHT | | | | |
| CC | and TNFSF6/FasL. Protects against apoptosis. | | | | |
| CC | - SUBCELLULAR LOCATION: Secreted. | | | | |
| CC | - TISSUE SPECIFICITY: Detected in fetal lung, brain and liver. | | | | |

34 7 2.3 214 1 YDHL_HSVS7 P25049 herpesvirus
35 7 2.3 230 1 RNSI_ARATH P42813 arabidopsis
36 7 2.3 235 1 CAS2_PIG P39036 sus scrofa
37 7 2.3 247 1 HXA4_HETER O91422 heterodontu
38 7 2.3 270 1 HIT7_ARATH P34047 arabidopsis
39 7 2.3 274 1 Y296_RICPR O92d41 rickettsia
40 7 2.3 277 1 Y495_MYCLE P54579 mycobacteri
41 7 2.3 283 1 TR14_HUMAN O92956 homo sapien
42 7 2.3 315 1 SPY2_HUMAN O43597 homo sapien
43 7 2.3 315 1 SPY2_MOUSE O9qvx8 mus musculu
44 7 2.3 333 1 TNR6_BOVIN P51867 bos taurus
45 7 2.3 332 1 TNR6_PIG O77736 sus scrofa

Detected in adult stomach, spinal cord, lymph node, trachea, spleen, colon and lung. Highly expressed in several primary tumors from colon, stomach, rectum, esophagus and in SW480 colon carcinoma cells.

-1- SIMILARITY: CONTAINS 4 TNFR-CYS REPEATS.

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CC
CC EMBL: AF104419; AAD03056.1; -
CC EMBL: AF134240; AAD29688.1; -
CC EMBL: AF217796; AAF35244.1; -
CC EMBL: AF217793; AAF33685.1; -
CC EMBL: AF217794; AAF33686.1; -
CC EMBL: AL121845; CAC03668.1; -
CC EMBL: BC017065; AAH17065.1; -
CC Genew: HGNC:11921; TNFRSF6B.
CC MIM: 603361; -
CC HSP: O14763; IDOC.
CC InterPro: IPR001368; TNFR_c6.
CC Pfam: PF00020; TNFR_c6; 4.
CC ProDom: PD000771; TNFR_c6; 1.
CC SMART: SM00208; TNFR_3.
DR PROSITE: PS00652; TNFR_NCFR_1; 2.
DR PROSITE: PS00650; TNFR_NCFR_2; 2.
KW Receptor; Apoptosis; Glycoprotein; Repeat; Signal.
FT SIGNAL 1 29
FT CHAIN 30 300
FT REPEAT 31 70
FT REPEAT 72 113
FT REPEAT 115 150
FT REPEAT 152 193
FT DISULFID 49 62
FT DISULFID 52 70
FT DISULFID 73 88
FT DISULFID 91 105
FT DISULFID 113 126
FT DISULFID 132 150
FT DISULFID 153 168
FT DISULFID 174 193
FT CARBOHYD 173 173
SQ SEQUENCE 300 AA; 32679 MW; F90AE33718449AF CRC64;

Query Match 100.0%; Score 300; DB 1; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.5e-273;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 MAAIAGPGSLICLVIALPVPVAVRVAETPTYPMDAETGELVCAQCPPTGVOR 60
DB 1 MAAIAGPGSLICLVIALPVPVAVRVAETPTYPMDAETGELVCAQCPPTGVOR 60
OY 61 PRRDSPPTCGPCPPPHYTFQFNWYLERCYCNVLCGEREEERACATNRRACRGTGFF 120
DB 61 PRRDSPPTCGPCPPPHYTFQFNWYLERCYCNVLCGEREEERACATNRRACRGTGFF 120
OY 121 AAAGFCLHASCPCGAGVIAPTPSQNTCCQPCPGTFSASSSSSSPCOPHNCTALGIA 180
DB 121 AAAGFCLHASCPCGAGVIAPTPSQNTCCQPCPGTFSASSSSSSPCOPHNCTALGIA 180
OY 181 LNVPGSSSHDTLCTCTGTPPLSTRVPGAECERAVIDFAFDISIKRLQLQALEADE 240
DB 181 LNVPGSSSHDTLCTCTGTPPLSTRVPGAECERAVIDFAFDISIKRLQLQALEADE 240
OY 241 GNGPPTPRAGRALQIKLRRLTELLGAQDQALLVRLQALRVARMGLERSVRRRLPVH 300
DB 241 GNGPPTPRAGRALQIKLRRLTELLGAQDQALLVRLQALRVARMGLERSVRRRLPVH 300

RESULT 2
TRLT HUMAN
ID TRLT HUMAN STANDARD; PRT: 430 AA.
AC Q969Z4; Q96JUL; Q9BUX7;
DT 15-JUN-2002 (Rel. 41, Created)
DT 15-JUN-2002 (Rel. 41, Last sequence update)
DT 15-JUN-2002 (Rel. 41, Last annotation update)
DE Tumor necrosis factor receptor superfamily member TNFRSF19L precursor
GN (Receptor expressed in lymphoid tissues).
GN TNFRSF19L OR RELT.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
OX NCBI_Taxid=9606;
RN [1]
RP SEQUENCE FROM N.A., AND SEQUENCE OF N-TERMINUS.
RC TISSUE-Lymphoma;
RX MEDLINE-21213541; PubMed-11313261;
RA Sica G.L., Zhu G., Tamada K., Liu D., Ni J., Chen L.;
RT "RELT, a new member of the tumor necrosis factor receptor superfamily,
RT is selectively expressed in hematopoietic tissues and activates
RT transcription factor NF-kappaB.";
RL Blood 97:2702-2707 (2001).
RN [2]
RP SEQUENCE FROM N.A.
RC TISSUE-Retinioblastoma;
RA Isogai T., Ota T., Hayashi K., Sugiyama T., Otsuki T., Suzuki Y.,
RA Nishikawa T., Nagai K., Sugano S., Shiratori A., Sudo H.,
RA Takagishima M., Hosoliri T., Kaku Y., Kodaira H., Kondo H., Sugawara M.,
RA Wakahashi M., Chiba Y., Ishida S., Murakami K., Ono Y., Takiguchi S.,
RA Watanabe S., Kimura K., Murakami K., Ishii S., Kawai Y., Saito K.,
RA Yamamoto J., Wakamatsu A., Nakamura Y., Nagahara K., Masuno Y.,
RA Niinomiya K., Iwayanagi T.;
RT "NEO human cDNA sequencing project.";
RL Submitted (May-2001) to the EMBL/Genbank/DBJ databases.
RN [3]
RP SEQUENCE FROM N.A.
RC TISSUE-Colon, and Eye;
RA Strausberg R.;
RL Submitted (Nov-2001) to the EMBL/Genbank/DBJ databases.
RN [4]
RP SEQUENCE OF 121-430 FROM N.A.
RC TISSUE-Spleen;
RA Jikuya H., Takano J., Nomura N., Kikuno R., Nagase T., Ohara O.;
RT "The nucleotide sequence of a long cDNA clone isolated from human
RT spleen.";
RL Submitted (JAN-2002) to the EMBL/Genbank/DBJ databases.
CC -1- FUNCTION: Mediates activation of NF-kappa-B. May play a role in T-
CC cell activation.
CC -1- SUBUNIT: Associates with TRAF1.
CC -1- SUBCELLULAR LOCATION: Type I membrane protein (Probable).
CC -1- TISSUE SPECIFICITY: Highest levels are in spleen, lymph node,
CC thymus, peripheral blood leukocytes, bone marrow and fetal liver.
CC Very low levels in skeletal muscle, testis and colon. Not detected
CC in brain, kidney and pancreas.
CC -1- SIMILARITY: CONTAINS 1 TNFR-CYS REPEAT.
CC -1- CAUTION: Ref.4 sequence differs from that shown due to several
CC frameshifts.

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CC
CC EMBL: AF319553; AAK77356.1; -
CC EMBL: AK027899; BAB55441.1; -
CC EMBL: BC001812; AAH01812.1; -
CC EMBL: BC017279; AAH17279.1; -


```

DR EMBL; AK074128; BAB84954.1; ALT_FRAME.
DR Genew; HGNC:13764; TNFRSF19L.
DR PROSITE; PS00652; TNFR_NGFR_1; FALSE_NEG.
DR PROSITE; PS00650; TNFR_NGFR_2; FALSE_NEG.
DR Receptor; Transmembrane; Glycoprotein; Signal.
FT SIGNAL 1 26
FT CHAIN 27 430
FT DOMAIN 27 162 TUMOR NECROSIS FACTOR RECEPTOR
FT TRANSMEM 163 183 SUPERFAMILY MEMBER TNFRSF19L.
FT DOMAIN 184 430 EXTRACELLULAR (POTENTIAL).
FT REPEAT 50 90 POTENTIAL.
FT DISULFID 51 65 CYTOPLASMIC (POTENTIAL).
FT CARBOHYD 71 90 TNFR-CYS.
FT CONFLICT 149 149 BY SIMILARITY.
FT CONFLICT 122 122 N-LINKED (GLCNAC. . .) (POTENTIAL).
FT CONFLICT 187 187 D -> S (IN REF. 4).
FT CONFLICT 273 273 K -> E (IN REF. 2).
FT CONFLICT 379 380 H -> R (IN REF. 2).
SQ SEQUENCE 430 AA; 46092 MW; 4A5AB9AE32D36101 CRC64;

Query Match
Best Local Similarity 3.0%; Score 9; DB 1; Length 430;
Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 152 PCPPTGTFSA 160
DB 50 PCPPTGTFSA 58

RESULT 3
TRIL_MACFA STANDARD; PRT; 430 AA.
ID TRIL_MACFA STANDARD; PRT; 430 AA.
AC Q9N092;
DT 15-JUN-2002 (Rel. 41, Created)
DT 15-JUN-2002 (Rel. 41, Last sequence update)
DT 15-JUN-2002 (Rel. 41, Last annotation update)
DE Tumor necrosis factor receptor superfamily member TNFRSF19L precursor
DE (Receptor expressed in lymphoid tissues).
GN TNFRSF19L OR RELT.
OS Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Cercopithecoidea;
OC Cercopithecoidea; Macaca.
OX NCBI_TaxID=9541;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Brain;
RX MEDLINE=21458551; PubMed=11574149;
RA Osada N., Hida M., Kusuda J., Tanuma R., Iseki K., Hirata M., Suto Y.,
RA Hirai M., Terao K., Suzuki Y., Sugano S., Hashimoto K., Kusuda J.;
RA "Assignment of 118 novel cDNAs of cynomolgus monkey brain to human
RA chromosomes.";
RL Gene 275:31-37(2001).
CC -1- FUNCTION: Mediates activation of NF-kappa-B (By similarity). May
CC play a role in T-cell activation.
CC -1- SUBUNIT: Associates with TRAF1 (By similarity).
CC -1- SUBCELLULAR LOCATION: Type I membrane protein (Probable).
CC -1- SIMILARITY: CONTAINS 1 TNFR-CYS REPEAT.
CC
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CC
CC EMBL; AB046039; BAB01621.1; -
CC InterPro; IPR001368; TNFR_C6.
CC PROSITE; PS00652; TNFR_NGFR_1; FALSE_NEG.
CC PROSITE; PS00650; TNFR_NGFR_2; FALSE_NEG.
CC SMART; SM00208; TNFR; 1.

```

```

KM Receptor; Transmembrane; Glycoprotein; Signal.
FT SIGNAL 1 26
FT CHAIN 27 430
FT DOMAIN 27 162 TUMOR NECROSIS FACTOR RECEPTOR
FT TRANSMEM 163 183 SUPERFAMILY MEMBER TNFRSF19L.
FT DOMAIN 184 430 EXTRACELLULAR (POTENTIAL).
FT REPEAT 50 90 POTENTIAL.
FT DISULFID 51 65 CYTOPLASMIC (POTENTIAL).
FT CARBOHYD 71 90 TNFR-CYS.
FT DISULFID 149 149 BY SIMILARITY.
FT DISULFID 149 149 N-LINKED (GLCNAC. . .) (POTENTIAL).
SQ SEQUENCE 430 AA; 45850 MW; BA8DE92593E1E859 CRC64;

Query Match
Best Local Similarity 3.0%; Score 9; DB 1; Length 430;
Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 152 PCPPTGTFSA 160
DB 50 PCPPTGTFSA 58

RESULT 4
OREX_CANFA STANDARD; PRT; 130 AA.
ID OREX_CANFA STANDARD; PRT; 130 AA.
AC Q9GLF6;
DT 16-OCT-2001 (Rel. 40, Created)
DT 16-OCT-2001 (Rel. 40, Last sequence update)
DT 15-JUN-2002 (Rel. 41, Last annotation update)
DE Orexin precursor (Hypocretin) (Hcrt) [Contains: Orexin-A (Hypocretin-
DE 1) (Hcrt1); Orexin-B (Hypocretin-2) (Hcrt2)].
GN HCRT OR OX OR PROX.
OS Canis familiaris (dog).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Carnivora; Fissipedia; Canidae; Canis.
OX NCBI_TaxID=9615;
RN [1]
RP SEQUENCE FROM N.A., AND VARIANT THR-30.
RX MEDLINE=21180003; PubMed=11282968;
RA Hungs M., Fan J., Lin L., Lin X., Mignot E.;
RA "Identification and functional analysis of mutations in the hypocretin
RA (orexin) genes of narcoleptic canines.";
RL Genome Res. 11:531-539(2001).
RN [2]
RP REVIEW.
RX MEDLINE=21237974; PubMed=11340621;
RA Hungs M., Mignot E.;
RL "Hypocretin/Orexin, sleep and narcolepsy.";
RL Bioessays 23:397-408(2001).
RN [3]
RP REVIEW.
RX MEDLINE=21178476; PubMed=11283317;
RA Willie J.T., Chemelli R.M., Sinton C.M., Yanagisawa M.;
RA "To eat or to sleep? Orexin in the regulation of feeding and
RA wakefulness.";
RL Annu. Rev. Neurosci. 24:429-458(2001).
CC -1- FUNCTION: Neuropeptides that play a significant role in the
CC regulation of food intake and sleep-wakefulness, possibly by
CC coordinating the complex behavioral and physiologic responses of
CC these complementary homeostatic functions. A broader role in the
CC homeostatic regulation of energy metabolism, autonomic function,
CC hormonal balance and the regulation of body fluids, is also
CC suggested. Orexin-A binds to both OX1R and OX2R with a high
CC affinity, whereas orexin-B binds only to OX2R with a similar high
CC affinity.
CC -1- SUBCELLULAR LOCATION: ASSOCIATED WITH PERIARIAL ROUGH ENDOPLASMIC
CC RETICULUM AS WELL AS CYTOPLASMIC LARGE GRANULAR VESICLES AT
CC SYNAPSES (BY SIMILARITY).
CC -1- PTM: SPECIFIC ENZYMOLOGIC CLEAVAGES AT PAIRED BASIC RESIDUES YIELD
CC THE DIFFERENT ACTIVE PEPTIDES.
CC -1- SIMILARITY: BELONGS TO THE OREXIN FAMILY.
CC -1- DATABASE: NAME-Protein Spotlight;
CC NOTE-Issue 15 of October 2001.

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CC WWW="http://www.expasy.org/spotlight/articles/split015.html".

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CC -----

DR EMBL: AF285110; AAC13965.1; -

DR InterPro: IPR001704; Orexin.

DR Pfam: PF02072; OREXIN.1.

DR PRINTS: PRO1091; OREXINP.

KW Neuropeptide; Cleavage on pair of basic residues; Signal; Amidation;

KW Polymorphism.

FT SIGNAL 1 32 BY SIMILARITY.

FT PEPTIDE 33 65 OREXIN-A.

FT PEPTIDE 69 96 OREXIN-B.

FT PROPEP 97 130

FT MOD_RES 33 33 PYRROLIDONE CARBOXYLIC ACID (BY

FT MOD_RES 65 65 SIMILARITY).

FT MOD_RES 65 65 AMIDATION (G-66 PROVIDE AMIDE GROUP) (BY

FT MOD_RES 96 96 SIMILARITY).

FT MOD_RES 96 96 AMIDATION (G-97 PROVIDE AMIDE GROUP) (BY

FT DISULFID 38 44 BY SIMILARITY).

FT DISULFID 39 46 BY SIMILARITY.

FT VARIANT 30 30 A -> T.

SO SEQUENCE 130 AA; 13328 MW; 2BF59D4C1EF422DF3 CRC64;

Query Match 2.7%; Score 8; DB 1; Length 130;

Best Local Similarity 100.0%; Pred. No. 3.1;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 228 RIQRLLQA 235

DB 78 RIQRLLQA 85

RESULT 5

OREX_MOUSE STANDARD; PRT; 130 AA.

AC 055241:

DT 30-MAY-2000 (Rel. 39, Created)

DT 30-MAY-2000 (Rel. 39, Last sequence update)

DT 15-JUN-2002 (Rel. 41, Last annotation update)

DE Orexin precursor (Hypocretin) (Hcrt) [Contains: Orexin-A (Hypocretin-1) (Hcrt1); Orexin-B (Hypocretin-2) (Hcrt2)].

GN Hcrt OR OX OR PROX.

OS Mus musculus (Mouse).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.

OX NCBI_TaxID=10090;

RN [1]

RP SEQUENCE FROM N.A.

RX MEDLINE=98150861; PubMed=9491897;

RA Sakurai T., Amemiya A., Ishii M., Matsuzaki I., Chemei R.M., Tanaka H., Williams S.C., Richardson J.A., Kozlowski G.P., Wilson S., Arch J.R.S., Buckingham R.E., Haynes A.C., Carr S.A., Annan R.S., Mancini D.E., Liu W.-S., Terrett J.A., Elshourbagy N.A., Beysma D.J., Yanagisawa M.

RA "Orexins and orexin receptors: a family of hypothalamic neuropeptides and G protein-coupled receptors that regulate feeding behavior."

RT Cell 92:573-585(1998).

RL [2]

RN SEQUENCE FROM N.A.

RP STRAIN=C57BL/6J.

RX MEDLINE=98081872; PubMed=9419374;

RA de Lecea L., Kilduff T.S., Peyron C., Gao X.-B., Foye P.E., Danielson P.E., Fukuhara C., Battenberg E.L.F., Gautvik V.T., Bartlett F.S. II, Frankel W.N., van den Pol A.N., Bloom F.E., Gautvik K.M., Sutcliffe J.G.;

RT "The hypocretins: hypothalamus-specific peptides with neuroexcitatory activity."

RT Proc. Natl. Acad. Sci. U.S.A. 95:322-327(1998).

RL [3]

RP REVIEW.

RX MEDLINE=21237974; PubMed=11340621;

RA Hungs M., Mignot E.;

RT "Hypocretin/orexin, sleep and narcolepsy."

RL Bioessays 23:397-408(2001).

RN [4]

RP REVIEW.

RX MEDLINE=21178476; PubMed=11283317;

RA Willie J.T., Chemelli R.M., Sinton C.M., Yanagisawa M.;

RT "To eat or to sleep? Orexin in the regulation of feeding and wakefulness."

RL Annu. Rev. Neurosci. 24:429-458(2001).

CC -1- FUNCTION: Neuropeptides that play a significant role in the regulation of food intake and sleep-wakefulness, possibly by coordinating the complex behavioral and physiologic responses of these complementary homeostatic functions. A broader role in the homeostatic regulation of energy metabolism, autonomic function, hormonal balance and the regulation of body fluids, is also suggested. Orexin-A binds to both OX1R and OX2R with a high affinity, whereas orexin-B binds only to OX2R with a similar high affinity.

CC -1- SUBCELLULAR LOCATION: ASSOCIATED WITH PERIKARYAL ROUGH ENDOPLASMIC RETICULUM AS WELL AS CYTOPLASMIC LARGE GRANULAR VESICLES AT SYNAPSES (BY SIMILARITY).

CC -1- TISSUE SPECIFICITY: RESTRICTED TO NEURONAL CELL BODIES OF THE DORSAL AND LATERAL HYPOTHALAMUS.

CC -1- PTM: SPECIFIC ENZYMAIC CLEAVAGES AT PAIRED BASIC RESIDUES YIELD AFFINITY.

CC -1- SIMILARITY: BELONGS TO THE OREXIN FAMILY.

CC -1- DATABASE: NAME-Protein Spotlight;

CC NOTE=Issue 15 of October 2001;

CC WWW="http://www.expasy.org/spotlight/articles/split015.html".

CC -----

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CC or send an email to license@isb-sdb.ch).

CC -----

DR EMBL: AF041242; AAC40040.1; -

DR EMBL: AF019566; AAC02934.1; -

DR MGD: MGI:1202306; Hcrt.

DR InterPro: IPR001704; Orexin.

DR Pfam: PF02072; OREXIN.1.

DR PRINTS: PRO1091; OREXINP.

KW Neuropeptide; Cleavage on pair of basic residues; Signal; Amidation.

KW SIGNAL 1 32 BY SIMILARITY.

FT PEPTIDE 33 65 OREXIN-A.

FT PEPTIDE 69 96 OREXIN-B.

FT PROPEP 97 130

FT MOD_RES 33 33 PYRROLIDONE CARBOXYLIC ACID (BY

FT MOD_RES 65 65 SIMILARITY).

FT MOD_RES 65 65 AMIDATION (G-66 PROVIDE AMIDE GROUP) (BY

FT MOD_RES 96 96 SIMILARITY).

FT MOD_RES 96 96 AMIDATION (G-97 PROVIDE AMIDE GROUP) (BY

FT DISULFID 38 44 BY SIMILARITY).

FT DISULFID 39 46 BY SIMILARITY.

SO SEQUENCE 130 AA; 13503 MW; D3C223FE8E835F1C CRC64;

Query Match 2.7%; Score 8; DB 1; Length 130;

Best Local Similarity 100.0%; Pred. No. 3.1;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 228 RIQRLLQA 235

DB 78 RIQRLLQA 85

RESULT 6
OREX_RAT STANDARD: PRT: 130 AA.
AC 055232;
DT 30-MAY-2000 (Rel. 39, Created)
DT 30-MAY-2000 (Rel. 39, Last sequence update)
DT 15-JUN-2002 (Rel. 41, Last annotation update)
DE Orexin precursor (Hypocretin) (Hcrt) [Contains: Orexin-A (Hypocretin-1) (Hcrt1); Orexin-B (Hypocretin-2) (Hcrt2)].
GN Hcrt OR OX OR PPOX.
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_TaxID=10116;
RN [1]
RP SEQUENCE FROM N.A., AND SEQUENCE OF 33-65 AND 69-96.
RC TISSUE=Brain;
RX MEDLINE=98150861; PubMed=9491897;
RA Sakurai T., Amemiya A., Ishii M., Matsuzaki I., Chemelli R.M., Arch J.R.S., Buckingham R.E., Haynes A.C., Carr S.A., Annan R.S., McNulty D.E., Liu W.-S., Terrett J.A., Elshourbagy N.A., Bergsma D.J., Yanagisawa M.;
RT "Orexins and orexin receptors: a family of hypothalamic neuropeptides and G protein-coupled receptors that regulate feeding behavior.";
RL Cell 92:573-585(1998).
RN [2]
RP SEQUENCE FROM N.A.
RC STRAIN=Sprague-Dawley;
RX MEDLINE=98081872; PubMed=9419374;
RA de Lecea L., Kilduff T.S., Peyron C., Gao X.-B., Foye P.E., Bartlett F.S. II, Frankel W.N., van den Pol A.N., Bloom F.E., Gautvik K.M., Sutcliffe J.G.;
RT "The hypocretins: hypothalamus-specific peptides with neuroexcitatory activity.";
RL Proc. Natl. Acad. Sci. U.S.A. 95:322-327(1998).
RN [3]
RP REVIEW.
RX MEDLINE=21237974; PubMed=11340621;
RA Hungs M., Mignot E.;
RT "Hypocretin/orexin, sleep and narcolepsy.";
RL Biosays 23:397-408(2001).
RN [4]
RP REVIEW.
RX MEDLINE=21178476; PubMed=11283317;
RA Willie J.T., Chemelli R.M., Sinton C.M., Yanagisawa M.;
RT "To eat or to sleep? Orexin in the regulation of feeding and wakefulness.";
RL Annu. Rev. Neurosci. 24:429-458(2001).
RN [5]
RP FUNCTION: Neuropeptides that play a significant role in the regulation of food intake and sleep-wakefulness, possibly by coordinating the complex behavioral and physiologic responses of these complementary homeostatic functions. A broader role in the homeostatic regulation of energy metabolism, autonomic function, hormonal balance and the regulation of body fluids, is also suggested. A modulation effect on luteinizing hormone-releasing hormone (LHRH) secretion also suggests a more minor contribution to the regulation of reproductive function. Orexin-A binds to both OX1R and OX2R with a high affinity, whereas orexin-B binds only to OX2R with a similar high affinity.
RN [6]
RP SUBCELLULAR LOCATION: ASSOCIATED WITH PERIKARYAL ROUGH ENDOPLASMIC RETICULUM AS WELL AS CYTOPLASMIC LARGE GRANULAR VESICLES AT SYNAPSES.
RN [7]
RP TISSUE SPECIFICITY: Produced by a small group of neurons restricted to the lateral and posterior hypothalamus and perifornical areas. Positive neurons project widely throughout the entire neuroaxis. Particularly abundant projections in the cerebral cortex, olfactory bulb, hippocampus, amygdala, septum, diagonal band of Broca, bed nucleus of the stria terminalis, thalamus, anterior and posterior hypothalamus, midbrain,

brainstem, and spinal cord. Immunoreactivity reported in the enteric nervous system and pancreas. In small amount, also detected in the testis.
CC -1- DEVELOPMENTAL STAGE: DETECTED AS EARLY AS EMBRYONIC DAY 18, BUT EXPRESSION INCREASED DRAMATICALLY AFTER THE THIRD POSTNATAL WEEK.
CC -1- INDUCTION: By nutritional state, up-regulated by fasting, fluid deprivation and insulin-induced hypoglycemia. Orexin-A immunoreactivity varies diurnally and peaks during the dark phase, in the pons and the location of locus coeruleus.
CC -1- PTM: SPECIFIC ENZYMATIC CLEAVAGES AT PAIRED BASIC RESIDUES YIELD THE DIFFERENT ACTIVE PEPTIDES.
CC -1- MASS SPECTROMETRY: MW=3558.7; MW_ERR=0.1; METHOD=MALDI; RANGE=33-65.
CC -1- SIMILARITY: BELONGS TO THE OREXIN FAMILY.
CC -1- DATABASE: NAME=protein Spotlight;
CC NOTE=Issue 15 of October 2001;
CC WWW="http://www.expasy.org/spotlight/articles/spl1015.html".
CC -----
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CC -----
DR EMBL; AF041241; AAC40039.1; -;
DR EMBL; AF019565; AAC02933.1; -;
DR InterPro; IPR001704; Orexin.
DR Pfam; PF02072; Orexin; 1.
DR PRINTS; PR01091; OREXINP.
KW Neuropeptide; Cleavage on pair of basic residues; Signal; Amidation.
FT SIGNAL 1 32
FT PEPTIDE 33 65 OREXIN-A.
FT PEPTIDE 69 96 OREXIN-B.
FT PROPEP 97 130
FT MOD_RES 33 33 PYRROLIDONE CARBOXYLIC ACID.
FT MOD_RES 65 65 AMIDATION (G-66 PROVIDE AMIDE GROUP).
FT MOD_RES 96 96 AMIDATION (G-97 PROVIDE AMIDE GROUP).
FT DISULFID 38 44
FT DISULFID 39 46
SQ SEQUENCE 130 AA: 00CAB259EDE2A404 CRC64;
SQ
Query Match 2.7%; Score 8; DB 1; Length 130;
Best Local Similarity 100.0%; Pred. No. 3.1;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
OY 228 RIQRRLQA 235
DB 78 RIQRRLQA 85
RESULT 7
OREX_HUMAN STANDARD: PRT: 131 AA.
AC 043612;
DT 30-MAY-2000 (Rel. 39, Created)
DT 30-MAY-2000 (Rel. 39, Last sequence update)
DT 15-JUN-2002 (Rel. 41, Last annotation update)
DE Orexin precursor (Hypocretin) (Hcrt) [Contains: Orexin-A (Hypocretin-1) (Hcrt1); Orexin-B (Hypocretin-2) (Hcrt2)].
GN Hcrt OR OX OR PPOX OR PPORX.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Homiidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=98150861; PubMed=9491897;
RA Sakurai T., Amemiya A., Ishii M., Matsuzaki I., Chemelli R.M., Tanaka H., Williams S.C., Richardson J.A., Kozlowski G.P., Wilson S., Arch J.R.S., Buckingham R.E., Haynes A.C., Carr S.A., Annan R.S., McNulty D.E., Liu W.-S., Terrett J.A., Elshourbagy N.A., Bergsma D.J.,

RA Yanagisawa M.;
 RT "Orexins and orexin receptors: a family of hypothalamic neuropeptides
 RL and G protein-coupled receptors that regulate feeding behavior.";
 RN Cell 92:573-585(1998).
 RP SEQUENCE FROM N.A.
 RX MEDLINE-99292744; PubMed-10364220;
 RA Sakurai T., Moriyuchi T., Furuya K., Kajiwara N., Nakamura T.,
 RT Yanagisawa M., Goto K.;
 RL "Structure and function of human prepro-orexin gene.";
 RN J. Biol. Chem. 274:17771-17776(1999).
 RP [3]
 RX STRUCTURE BY NMR OF 70-97.
 RA MEDLINE-20050594; PubMed-10583376;
 RT Lee J.-H., Bang E., Chae K.-J., Kim J.-Y., Lee D.W., Lee W.;
 RL "Solution structure of a new hypothalamic neuropeptide, human
 Eur. J. Biochem. 266:831-839(1999).
 RN [4]
 RP REVIEW.
 RX MEDLINE-21237974; PubMed-11340621;
 RA Hungs M., Mignot E.;
 RL "Hypocretin/orexin, sleep and narcolepsy.";
 RN Bioessays 23:397-408(2001).
 RP [5]
 RX REVIEW.
 RA MEDLINE-21178476; PubMed-11283317;
 RL Willie J.T., Chemelli R.M., Sinton C.M., Yanagisawa M.;
 RT "To eat or to sleep? Orexin in the regulation of feeding and
 wakefulness.";
 RN Annu. Rev. Neurosci. 24:429-458(2001).
 RP [6]
 RX VARIANT EARLY-ONSET NARCOLEPSY ARG-16, AND MUTAGENESIS OF LEU-16.
 RA MEDLINE-20429525; PubMed-10973318;
 RA Neyron C., Faraco J., Rogers W., Ripley B., Overeem S., Charney Y.,
 RA Nevelingova S., Aldrich M., Reynolds D., Albin R., Li R., Hungs M.,
 RA Pedrazzoli M., Padigaru M., Kucherlapati R., Fan J., Maki R.,
 RA Lammers G.J., Bouras C., Kucherlapati R., Nishino S., Mignot E.;
 RT "A mutation in a case of early onset narcolepsy and a generalized
 absence of hypocretin peptides in human narcoleptic brains.";
 RL Nat. Med. 6:991-997(2000).
 CC -1- FUNCTION: Neuropeptides that play a significant role in the
 regulation of food intake and sleep-wakefulness, possibly by
 coordinating the complex behavioral and physiologic responses of
 these complementary homeostatic functions. A broader role in the
 homeostatic regulation of energy metabolism, autonomic function,
 hormonal balance and the regulation of body fluids, is also
 suggested. Orexin-A binds to both OX1R and OX2R with a high
 affinity, whereas orexin-B binds only to OX2R with a similar high
 affinity.
 CC -1- SUBCELLULAR LOCATION: ASSOCIATED WITH PERIKARYAL ROUGH ENDOPLASMIC
 RETICULUM AS WELL AS CYTOPLASMIC LARGE GRANULAR VESICLES AT
 SYNAPSES (BY SIMILARITY).
 CC -1- TISSUE SPECIFICITY: ABUNDANTLY EXPRESSED IN SUBTHALAMIC NUCLEUS
 BUT UNDETECTABLE IN OTHER BRAIN REGIONS TESTED (HYPOTHALAMIC WAS
 NOT TESTED) AND IN HEART, PLACENTA, LUNG, LIVER, SKELETAL MUSCLE,
 KIDNEY AND PANCREAS.
 CC -1- PTM: SPECIFIC ENZYMATIC CLEAVAGES AT PAIRED BASIC RESIDUES YIELD
 THE DIFFERENT ACTIVE PEPTIDES.
 CC -1- DISEASE: Defects in HCR1 are a cause of narcolepsy, a neurological
 disabling sleep disorder, characterized by excessive daytime
 sleepiness, sleep fragmentation, symptoms of abnormal rapid-eye-
 movement (REM) sleep, such as cataplexy, hypnagogic
 hallucinations, and sleep paralysis. Cataplexy is a sudden loss of
 muscle tone triggered by emotions, which is the most valuable
 clinical feature used to diagnose narcolepsy. Human narcolepsy is
 associated with a deficient orexin system. Orexins are absent
 and/or greatly diminished in the brain and cerebrospinal fluid
 (CSF) of most narcoleptic patients. Human narcolepsy is primarily
 a sporadically occurring disorder but familial clustering has been
 observed.
 CC -1- SIMILARITY: BELONGS TO THE OREXIN FAMILY.
 CC -1- DATABASE: NAME-Protein Spotlight;

CC NOTE-Issue 15 of October 2001:
 CC WWW="http://www.expasy.org/spotlight/articles/spilt015.html".
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 CC -----
 DR EMBL: AF041240; AAC39600.1; -;
 DR EMBL: AF118885; AAD24459.1; -;
 DR PDB: 1CO0; 12-JAN-00.
 DR Genbank: HGNC:4847; HCRT.
 DR MIM: 602358; -;
 DR MIM: 161400; -;
 DR InterPro: IPR001704; Orexin.
 DR Pfam: PF02072; Orexin; 1.
 DR PRINTS: PR01091; OREXINP.
 DR Neuropeptide; Cleavage on pair of basic residues; Signal; Amidation;
 KW Disease mutation; 3D-structure.
 FT SIGNAL 1 33
 FT PEPTIDE 34 66
 FT PEPTIDE 70 97
 FT PROPEP 98 131
 FT MOD_RES 34 34
 FT MOD_RES 66 66
 FT MOD_RES 97 97
 FT MOD_RES 97 97
 FT DISULFID 39 45
 FT DISULFID 40 47
 FT VARIANT 16 16
 FT VARIANT 16 16
 FT MUTAGEN 16 16
 FT SEQUENCE 131 AA; 13363 MW; 139D9C33E9E4EF1 CRC64;
 SQ
 Query Match 2.7%; Score 8; DB 1; Length 131;
 Best local similarity 100.0%; Pred. No. 3.1;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 228 RLQRLQA 235
 DB 79 RLQRLQA 86
 RESULT 8
 OREX_PIG STANDARD; PRT; 131 AA.
 ID OREX_PIG
 AC 077668; O9TTA6;
 DT 30-MAY-2000 (Rel. 39, Created)
 DT 30-MAY-2000 (Rel. 39, Last sequence update)
 DT 15-JUN-2002 (Rel. 41, Last annotation update)
 DE Orexin precursor (Hypocretin) (HCRT) [Contains: Orexin-A (Hypocretin-
 DE 1) (Hcr1); Orexin-B (Hypocretin-2) (Hcr2)].
 GN HCRT OR OX OR PPOX.
 OS Sus scrofa (Pig).
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Cetartiodactyla; Suidae; Suidae; Sus.
 OC NCBI_TaxID=9823;
 RN [1]
 RP SEQUENCE FROM N.A., AND SYNTHESIS OF OREXIN-B.
 RC TISSUE-Hypothalamus;
 RX MEDLINE-99273584; PubMed-10343916;
 RA Dyer C.J., Touchette K.J., Carroll J.A., Allee G.L., Matteri R.L.;
 RT "Cloning of porcine prepro-orexin cDNA and effects of an intramuscular
 RT injection of synthetic porcine orexin-B on feed intake in young
 RT pigs.";
 RL Domest. Anim. Endocrinol. 16:145-148(1999).
 RN [2]

RP SEQUENCE OF 3-131 FROM N.A.
RA Malek M. Marklund S., Rothschild M.F.:
RT "Linkage and physical mapping of the porcine prepro-orexin gene."
RL Submitted (JUL-1999) to the EMBL/Genbank/DBJ databases.
CC -1- FUNCTION: Neuropeptides that play a significant role in the
CC regulation of food intake and sleep-wakefulness, possibly by
CC coordinating the complex behavioral and physiologic responses of
CC these complementary homeostatic functions. A broader role in the
CC homeostatic regulation of energy metabolism, autonomic function,
CC hormonal balance and the regulation of body fluids, is also
CC suggested. Orexin-A binds to both OX1R and OX2R with a high
CC affinity, whereas orexin-B binds only to OX2R with a similar high
CC affinity (by similarity).
CC -1- SUBCELLULAR LOCATION: ASSOCIATED WITH PERIKARAL ROUGH ENDOPLASMIC
CC RETICULUM AS WELL AS CYTOPLASMIC LARGE GRANULAR VESICLES AT
CC SYNAPSES (BY SIMILARITY).
CC -1- PTM: SPECIFIC ENZYMATIC CLEAVAGES AT PAIRED BASIC RESIDUES YIELD
CC THE DIFFERENT ACTIVE PEPTIDES.
CC -1- SIMILARITY: BELONGS TO THE OREXIN FAMILY.
CC -1- DATABASE: NAME-Protein Spotlight;
CC NOTE-Issue 15 of October 2001;
CC WWW="http://www.expasy.org/spotlight/articles/spllt015.html".
CC -----
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CC -----
DR EMBL; AF075241; AAC26827.1; -
DR EMBL; AF169352; AAC24216.1; -
DR InterPro; IPR001704; Orexin.
DR Pfam; PF02072; Orexin; 1.
DR PRINTS; PR01091; OREXINP.
KW Neuropeptide; Cleavage on pair of basic residues; Signal; Amidation.
FT SIGNAL 1 33 BY SIMILARITY.
FT PEPTIDE 34 66 OREXIN-A.
FT PEPTIDE 70 97 OREXIN-B.
FT PROPEP 98 131
FT MOD_RES 34 34
FT MOD_RES 66 66 PYROGLUTAMIC CARBOXYLIC ACID (BY
FT MOD_RES 97 97 AMIDATION (G-67 PROVIDE AMIDE GROUP) (BY
FT MOD_RES 97 97 SIMILARITY).
FT DISULFID 39 45 AMIDATION (G-98 PROVIDE AMIDE GROUP) (BY
FT DISULFID 40 47 SIMILARITY).
FT SEQUENCE 131 AA; 13457 MW; 665AV4448429AB1P CRC64;
SO
Query Match 2.7%; Score 8; DB 1; Length 131;
Best Local Similarity 100.0%; Pred. No. 3,1;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
OY 228 RLORLQA 235
DB 79 RLORLQA 86
RESULT 9
CAS2_RAT ID CAS2_RAT STANDARD; PRT; 179 AA.
AC P02667;
DT 21-JUL-1986 (Rel. 01, Created)
DT 21-JUL-1986 (Rel. 01, Last sequence update)
DT 16-OCT-2001 (Rel. 40, Last annotation update)
DE Gamma casein precursor.
GN CSNG.
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_TaxID=10116;

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RN [1]
RE SEQUENCE FROM N.A.
RX MEDLINE=83143278; PubMed=6298707;
RA Hobbs A.A., Rosen J.M.;
RT "Sequence of rat alpha- and gamma-casein mRNAs: evolutionary
RL comparison of the calcium-dependent rat casein multigene family.";
RN Nucleic Acids Res. 10:8079-8098(1982).
CC -!- FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT
CC CALCIUM PHOSPHATE.
CC -!- SUBCELLULAR LOCATION: Extracellular.
CC -!- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.
CC -!- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.
CC -----
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CC -----
CC EMBL, J00712; -; NOT_ANNOTATED_CDS.
CC -----
DR PIR: A03111; KGRF.
DR InterPro: IPR001588; Casein.
DR Pfam, PF00363; caseins; 1.
DR PROSITE; PS00306; CASEIN_ALPHA_BETA; 1.
DR Milk; Phosphorylation; signal.
FT SIGNAL 1 15
FT CHAIN 16 179 GAMMA CASEIN.
FT MOD_RES 24 24 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 25 25 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 52 52 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 53 53 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 54 54 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 55 55 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 56 56 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 59 59 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 60 60 PHOSPHORYLATION (POTENTIAL).
SQ SEQUENCE 179 AA; 20277 MW; 91B3EB95229976FD CRC64;
Query Match 2.7%; Score 8; DB 1; Length 179;
Best Local Similarity 100.0%; Pred. No. 4.1;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 159 SASSSSSE 166
DB 50 SASSSSSE 57
RESULT 10
CAS3_MOUSE
ID CAS3_MOUSE STANDARD; PRT; 184 AA.
AC 002862;
DT 01-JUN-1994 (Rel. 29, Created)
DT 01-JUN-1994 (Rel. 29, Last sequence update)
DT 16-OCT-2001 (Rel. 40, Last annotation update)
DE Gamma casein precursor (PP22).
GN CSNG.
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_TaxID=10090;
RX [1]
RP SEQUENCE FROM N.A. AND PARTIAL SEQUENCE.
RA MEDLINE=93320737; PubMed=7763793;
RA Sasaki T., Sasaki M., Enami J.;
RT "Mouse gamma-casein cDNA: PCR cloning and sequence analysis.";
RL Zool. Sci. 10:65-72(1993).
CC -!- FUNCTION: IMPORTANT ROLE IN THE CAPACITY OF MILK TO TRANSPORT
CC CALCIUM PHOSPHATE.
CC -!- SUBCELLULAR LOCATION: Extracellular.
CC -!- TISSUE SPECIFICITY: MAMMARY GLAND; MILK.
CC -!- SIMILARITY: BELONGS TO THE ALPHA-CASEIN FAMILY.
CC -----

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CC or send an email to license@sib-sib.ch).

DR EMBL: D10215; BAA01067.1; -
DR MGD: MGI:88542; Ccng
DR InterPro: IPR001588; Casein.
DR Pfam: PF00363; caseins; 1.
KW Milk; Phosphorylation; signal.
FT SIGNAL 1 15
FT CHAIN 16 184 GAMMA CASEIN.
FT MOD_RES 23 23 PHOSPHORYLATION.
FT MOD_RES 24 24 PHOSPHORYLATION.
FT MOD_RES 25 25 PHOSPHORYLATION.
FT MOD_RES 37 37 PHOSPHORYLATION.
FT MOD_RES 53 53 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 54 54 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 55 55 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 56 56 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 57 57 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 60 60 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 61 61 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 71 71 PHOSPHORYLATION (POTENTIAL).
FT MOD_RES 88 88 PHOSPHORYLATION (POTENTIAL).
SQ SEQUENCE 184 AA; 21100 MW; ABE6C45FD3E2A32 CRC64;

Query Match 2.7%; Score 8; DB 1; Length 184;
Best Local Similarity 100.0%; Pred. No. 4.2;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 159 SASSSSSE 166
DB 51 SASSSSSE 58

RESULT 11
ADRO_MOUSE
ID ADRO_MOUSE STANDARD; PRT; 494 AA.
AC 061578;
DT 15-JUL-1998 (Rel. 36, Created)
DT 15-JUL-1998 (Rel. 36, Last sequence update)
DT 16-OCT-2001 (Rel. 40, Last annotation update)
DE NADPH:adrenodoxin oxidoreductase, mitochondrial precursor
DE (EC 1.18.1.2) (Adrenodoxin reductase) (AR) (Ferredoxin-NADP(+)
DE reductase).
GN FDXR.
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Mus.
OX NCBI_TaxID=10090;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=C57BL/6; TISSUE=Kidney;
RX MEDLINE=96085117; PubMed=7495857;
RA Itoh S., Iemura O., Yamada E., Yoshimura T., Tsujikawa K., Kohana Y.,
RA Mimura Y.;
RT "cDNA cloning of mouse ferredoxin reductase from kidney."
RL Biochim. Biophys. Acta 1264:159-162(1995).
CC -!- FUNCTION: SERVES AS THE FIRST ELECTRON TRANSFER PROTEIN IN ALL THE
CC MITOCHONDRIAL P450 SYSTEMS, INCLUDING CHOLESTEROL SIDE CHAIN
CC CLEAVAGE IN ALL STEROIDGENIC TISSUES, STEROID 11-BETA
CC HYDROXYLATION IN THE ADRENAL CORTEX, 25-OH-VITAMIN D3-24
CC HYDROXYLATION IN THE KIDNEY, AND STEROL C-27 HYDROXYLATION IN THE
CC LIVER.
CC -!- CATALYTIC ACTIVITY: Reduced adrenodoxin + NADP(+) = oxidized
CC adrenodoxin + NADPH.
CC -!- CORFACTOR: FAD.
CC -!- PATHWAY: CHOLESTEROL SIDE-CHAIN-CLEAVAGE SYSTEM.

CC -!- SUBCELLULAR LOCATION: Mitochondrial matrix.
CC -!- TISSUE SPECIFICITY: EXPRESSED IN THE ADRENAL, TESTIS AND OVARY AND
CC TO A LESSER EXTENT IN THE LIVER AND KIDNEY.

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CC or send an email to license@sib-sib.ch).

DR EMBL: D49920; BAA08659.1; -
DR HSSP: P08165; 1E6E.
DR MGD: MGI:104724; Fdxr.
DR InterPro: IPR000759; Adrxn_reductase.
DR PRINTS: PR00419; ADXREDTASE.
KW Electron transport; Oxidoreductase; Flavoprotein; NADP; FAD;
KW Mitochondrion; Transil peptide.
FT TRANSIT 1 34
FT CHAIN 35 494 MITOCHONDRION (POTENTIAL).
SQ SEQUENCE 494 AA; 54202 MW; 4BD279DFC606A5C5 CRC64;

Query Match 2.7%; Score 8; DB 1; Length 494;
Best Local Similarity 100.0%; Pred. No. 10;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 258 RRRLELL 265
DB 276 RRRLELL 283

RESULT 12
YDEV_ECOLI
ID YDEV_ECOLI STANDARD; PRT; 530 AA.
AC P77432; Q99894;
DT 01-NOV-1997 (Rel. 35, Created)
DT 01-NOV-1997 (Rel. 35, Last sequence update)
DT 16-OCT-2001 (Rel. 40, Last annotation update)
DE Hypothetical sugar kinase ydev.
DE YDEV OR B1511.
GN YDEV OR B1511.
OS Escherichia coli.
OC Bacteria; Proteobacteria; gamma subdivision; Enterobacteriaceae;
OC Escherichia.
OX NCBI_TaxID=562;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=K12 / MG1655;
RX MEDLINE=97426617; PubMed=9278503;
RA Blattner F.R., Plunkett G., III, Bloch C.A., Perna N.T., Burland V.,
RA Riley M., Collado-Vides J., Glasner J.D., Rode C.K., Mayhew G.F.,
RA Gregor J., Davis N.W., Kirkpatrick H.A., Goeden M.A., Rose D.J.,
RA Mau B., Shao Y.;
RT "The complete genome sequence of Escherichia coli K-12."
RL Science 277:1453-1474(1997).
RN [2]
RP SEQUENCE FROM N.A.
RC STRAIN=K12;
RX MEDLINE=9751357; PubMed=9097039;
RA Alth H., Baba T., Fujita K., Hayashi K., Inada T., Isono K.,
RA Itoh T., Kasai H., Kashimoto K., Kimura S., Kitakawa M.,
RA Kitagawa M., Makino K., Miki T., Mizobuchi K., Mori H., Mori T.,
RA Motomura K., Nakase S., Nakamura Y., Nashimoto H., Nishio Y.,
RA Oshima T., Saito N., Sampei G., Seki Y., Sivasubram S.,
RA Tagami H., Takeda J., Takemoto K., Takeuchi Y., Wada C.,
RA Yamamoto Y., Horiuchi T.;
RT "A 570-kb DNA sequence of the Escherichia coli K-12 genome
RT corresponding to the 28.0-40.1 min region on the linkage map."
RL DNA Res. 3:363-377(1996).
RN [3]
RP SEQUENCE OF 182-495 FROM N.A.
RX MEDLINE=96243037; PubMed=8649811;
RA Das R., Reddy E.P., Chatterjee D., Andrews D.W.;

RT "Identification of a novel Bcl-2 related gene, BRAG-1, in human
 RT glioma.";
 RL Oncogene 12:947-951(1996).
 CC -1- SIMILARITY: BELONGS TO THE FUCOKINASE / GLUCONOKINASE /
 CC GLYCEROKINASE / XYLOKINASE FAMILY.
 CC -1- CAUTION: WAS THOUGHT BY REF.3 TO BE A HUMAN SEQUENCE AND WAS
 CC CALLED BY THEM BRAG1 (BRAIN-RELATED APOPTOSIS GENE) (BRAG-1)
 CC WITH A ROLE IN APOPTOSIS. THE DNA SEQUENCE OF THE REGION THEY
 CC SEQUENCED IS MORE THAN 99% IDENTICAL TO THAT OF THIS E.COLI
 CC GENE. FURTHERMORE THEY CLAIM 'EXTENSIVE SIMILARITY TO THE
 CC BCL-2 FAMILY OF GENES.' SUCH A SIMILARITY IS NOT SIGNIFICANT
 CC AND THIS PROTEIN IS MUCH MORE LIKELY TO BE A SUGAR KINASE.
 CC -----
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 CC -----
 DR EMBL; AE000248; AAC74584.1; -
 DR EMBL; D90793; BA15191.1; -
 DR EMBL; D90794; BA15198.1; -
 DR EMBL; S82185; AAC17184.1; -
 DR EcoGene; EG13804; ydev.
 DR InterPro: IPR000577; FGGY_kin.
 DR Pfam; PF00370; FGGY_1.
 DR Pfam; PF02782; FGGY_C_1.
 DR PROSITE; PS00933; FGGY_KINASES_1; FALSE_NEG.
 DR PROSITE; PS00445; FGGY_KINASES_2; FALSE_NEG.
 KW Hypothetical protein; Transferase; Kinase; Complete proteome.
 FT CONFLICT 490 495 PDPKX -> TRPKA (IN REF. 2).
 SQ SEQUENCE 530 AA; 57544 MW; CEC3B1E7C8982063 CRC64;
 Query Match 2.7%; Score 8; DB 1; Length 530;
 Best Local Similarity 100.0%; Pred. No. 11;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 Oy 41 AETGERLY 48
 Db 475 AETGERLY 482
 RESULT 13
 GLMS_NOSS9 STANDARD; PRT; 626 AA.
 AC 068280;
 DT 30-MAY-2000 (Rel. 39, Created)
 DT 30-MAY-2000 (Rel. 39, Last sequence update)
 DT 15-JUN-2002 (Rel. 41, Last annotation update)
 DE Glucosamine--fructose-6-phosphate aminotransferase [isomerizing]
 DE (EC 2.6.1.16) (hexosephosphate aminotransferase) (D-fructose-6-
 DE phosphate amidotransferase) (GFAT) (L-glutamine-D-fructose-6-phosphate
 DE amidotransferase) (Glucosamine-6-phosphate synthase).
 GN GLMS OR NODM.
 OS Nostoc sp. (strain PCC 9229).
 OC Bacteria; Cyanobacteria; Nostocales; Nostocaceae; Nostoc.
 OX NCBI_TaxID=70817;
 RN [1]
 RA SEQUENCE FROM N.A.
 RA Vileiro A., Matveyev A., Rasmussen U., Bergman B.;
 RT "Characterization of a nodM homologous gene in the symbiotic
 RT cyanobacterium Nostoc PCC 9229".
 RL Submitted (Oct-1997) to the EMBL/GenBank/DBJ databases.
 CC -1- FUNCTION: CATALYZES THE FIRST STEP IN HEXOSAMINE METABOLISM,
 CC CONVERTING FRUCTOSE-6P INTO GLUCOSAMINE-6P USING GLUTAMINE AS A
 CC NITROGEN SOURCE (BY SIMILARITY).
 CC -1- CATALYTIC ACTIVITY: L-glutamine + D-fructose 6-phosphate -> L-
 CC glutamate + D-glucosamine 6-phosphate.
 CC -1- SUBCELLULAR LOCATION: Cytoplasmic (by similarity).
 CC -1- SIMILARITY: IN THE C-TERMINAL SECTION; BELONGS TO THE SIS FAMILY.
 CC GFAT SUBFAMILY.

CC -1- SIMILARITY: CONTAINS 1 TYPE-2 GLUTAMINE AMIDOTRANSFERASE DOMAIN.
 CC -----
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 CC -----
 DR EMBL; AF028734; AAC17973.1; -
 DR HSSP; P17169; IGDO.
 DR MEROPS; C44.971; -
 DR InterPro: IPR000583; GATase_2.
 DR InterPro: IPR001347; SIS.
 DR Pfam; PF00310; GATase_2; 1.
 DR Pfam; PF01380; SIS; 2.
 DR TIGRfams; TIGR01135; gims; 1.
 DR PROSITE; PS00443; GATASE_TYPE_II; 1.
 KW Transferase; Aminotransferase; Glutamine amidotransferase.
 FT INT_MET 0 0
 FT ACT_SITE 1 1
 FT ACT_SITE 621 621 ISOMERIZATION FRD-6P (BY SIMILARITY).
 FT DOMAIN 1 187 GLUTAMINE AMIDOTRANSFERASE.
 SQ SEQUENCE 626 AA; 68638 MW; 415FCF5046F2F103 CRC64;
 Query Match 2.7%; Score 8; DB 1; Length 626;
 Best Local Similarity 100.0%; Pred. No. 12;
 Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 Oy 158 FSASSSSS 165
 Db 138 FSASSSSS 145
 RESULT 14
 TSP2_HUMAN STANDARD; PRT; 1172 AA.
 ID TSP2_HUMAN
 AC P35442;
 DT 01-JUN-1994 (Rel. 29, Created)
 DT 01-JUN-1994 (Rel. 29, Last sequence update)
 DT 16-OCT-2001 (Rel. 40, Last annotation update)
 DE Thrombospondin 2 precursor.
 GN THBS2 OR TSP2.
 OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 CC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 OX NCBI_TaxID=9606;
 RN [1]
 RA SEQUENCE FROM N.A.
 RA MEDLINE=94010892; PubMed=8406456;
 RA Label1 T.V., Byers P.H.;
 RT "Sequence and characterization of the complete human thrombospondin 2
 RT cDNA: potential regulatory role for the 3' untranslated region.";
 RL Genomics 17:225-229(1993).
 RN [2]
 RP SEQUENCE OF 560-1172 FROM N.A.
 RP TISSUE=fibroblast;
 RC MEDLINE=92217961; PubMed=1559694;
 RA Label1 T.V., McGookey Milewicz D.J., Distche C.M., Byers P.H.;
 RT "Thrombospondin II: partial cDNA sequence, chromosome location, and
 RT expression of a second member of the thrombospondin gene family in
 RT humans.";
 RL Genomics 12:421-429(1992).
 CC -1- FUNCTION: ADHESIVE GLYCOPROTEIN THAT MEDIATES CELL-TO-CELL AND
 CC CELL-TO-MATRIX INTERACTIONS. CAN BIND TO FIBRINOGEN, FIBRONECTIN,
 CC LAMININ AND TYPE V COLLAGEN.
 CC -1- SUBUNIT: HOMOTRIMER; DISULFIDE-LINKED.
 CC -1- SIMILARITY: BELONGS TO THE THROMBOSPONDIN FAMILY.
 CC -1- SIMILARITY: CONTAINS 1 WFC DOMAIN.
 CC -1- SIMILARITY: CONTAINS 3 EGF-LIKE DOMAINS.
 CC -1- SIMILARITY: CONTAINS 3 TSP TYPE-1 DOMAINS.
 CC -1- SIMILARITY: CONTAINS 7 TSP TYPE-3 DOMAINS.

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OM protein - protein search, using sw model

Run on: July 16, 2003, 19:39:04 ; Search time 33 Seconds
(Without alignments)
1873.156 Million cell updates/sec

Title: US-09-935-727-2
Perfect score: 300
Sequence: 1 MRALEGPGLSLCLVLPALP.....RVARMPLERSVREPLPVH 300

Scoring table:
Gapop 60.0 , Gapext 60.0

Searched: 671580 seqs, 206047115 residues

Word size : 0

Total number of hits satisfying chosen parameters: 671580

Minimum DB seq length: 0

Maximum DB seq length: 200000000

Post-processing: Listing first 45 summaries

Database :

SPTREMBL_21:*
1: sp_archaea:*
2: sp_bacteria:*
3: sp_fungi:*
4: sp_human:*
5: sp_invertebrate:*
6: sp_mammal:*
7: sp_mhc:*
8: sp_organelle:*
9: sp_phage:*
10: sp_plant:*
11: sp_rodent:*
12: sp_virus:*
13: sp_vertebrate:*
14: sp_unclassified:*
15: sp_virus:*
16: sp_bacteriap:*
17: sp_archaeap:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | Query Match | Length | ID | Description |
|------------|-------|-------------|--------|----|-------------|
| 1 | 10 | 3.3 | 343 | 5 | Q95003 |
| 2 | 9 | 3.0 | 327 | 16 | Q91443 |
| 3 | 9 | 3.0 | 561 | 10 | Q95H82 |
| 4 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 5 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 6 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 7 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 8 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 9 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 10 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 11 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 12 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 13 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 14 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 15 | 8 | 2.7 | 54 | 12 | Q95H82 |
| 16 | 8 | 2.7 | 54 | 12 | Q95H82 |

| | | | | | | |
|----|---|-----|-----|----|--------|---------------------|
| 17 | 8 | 2.7 | 54 | 12 | Q95002 | 089902 budgerigar |
| 18 | 8 | 2.7 | 54 | 12 | Q95003 | 089903 budgerigar |
| 19 | 8 | 2.7 | 54 | 12 | Q95004 | 089904 budgerigar |
| 20 | 8 | 2.7 | 54 | 12 | Q95005 | 089905 budgerigar |
| 21 | 8 | 2.7 | 66 | 6 | Q95L34 | 095134 ovis aries |
| 22 | 8 | 2.7 | 71 | 2 | Q93M44 | Q93M44 bordetella |
| 23 | 8 | 2.7 | 145 | 12 | Q91BL0 | Q91BL0 budgerigar |
| 24 | 8 | 2.7 | 145 | 12 | Q9WC04 | Q9WC04 budgerigar |
| 25 | 8 | 2.7 | 181 | 10 | Q65446 | Q65446 arabidopsis |
| 26 | 8 | 2.7 | 191 | 16 | Q8XG64 | Q8XG64 escherichia |
| 27 | 8 | 2.7 | 206 | 2 | Q9X6H9 | Q9X6H9 streptococc |
| 28 | 8 | 2.7 | 241 | 10 | Q49719 | Q49719 arabidopsis |
| 29 | 8 | 2.7 | 269 | 4 | Q9GZ47 | Q9GZ47 homo sapien |
| 30 | 8 | 2.7 | 297 | 16 | Q8CZ47 | Q8CZ47 yerania pe |
| 31 | 8 | 2.7 | 299 | 4 | Q9H192 | Q9H192 homo sapien |
| 32 | 8 | 2.7 | 308 | 11 | Q923G5 | Q923G5 rattus norv |
| 33 | 8 | 2.7 | 308 | 11 | Q91W06 | Q91W06 mus musculu |
| 34 | 8 | 2.7 | 341 | 5 | Q9XXL8 | Q9XXL8 caenorhabdi |
| 35 | 8 | 2.7 | 364 | 17 | Q8TWA8 | Q8TWA8 methanopyru |
| 36 | 8 | 2.7 | 440 | 2 | Q9JP96 | Q9JP96 rhodocycylus |
| 37 | 8 | 2.7 | 477 | 4 | Q9Y577 | Q9Y577 homo sapien |
| 38 | 8 | 2.7 | 493 | 4 | Q96DP2 | Q96DP2 homo sapien |
| 39 | 8 | 2.7 | 494 | 16 | Q8Z5S5 | Q8Z5S5 salmonella |
| 40 | 8 | 2.7 | 504 | 5 | Q9V4K7 | Q9V4K7 drosophila |
| 41 | 8 | 2.7 | 530 | 16 | Q8XAY5 | Q8XAY5 escherichia |
| 42 | 8 | 2.7 | 531 | 10 | Q9SPT3 | Q9SPT3 arabidopsis |
| 43 | 8 | 2.7 | 531 | 10 | Q42582 | Q42582 arabidopsis |
| 44 | 8 | 2.7 | 587 | 12 | Q9WC03 | Q9WC03 budgerigar |
| 45 | 8 | 2.7 | 599 | 12 | Q91BL1 | Q91BL1 budgerigar |

ALIGNMENTS

RESULT 1

Q95003 PRELIMINARY: PRT: 343 AA.
AC Q95003;
DT 01-DEC-2001 (TREMBLrel, 19, Created)
DT 01-DEC-2001 (TREMBLrel, 19, Last sequence update)
DT 01-JUN-2002 (TREMBLrel, 21, Last annotation update)
DE Y66D12A.12 protein.
GN Y66D12A.12.
OS Caenorhabditis elegans.
OC Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditioidea;
OC Rhabditidae; Peloderinae; Caenorhabditis.
OX NCBI_TaxID=6239;
RN [1]
RP SEQUENCE FROM N.A.
RA Submitted (OCT-2001) to the EMBL/GenBank/DBJ databases.
RN [2]
RP SEQUENCE FROM N.A.
RX MEDLINE=99069613; PubMed=9851916;
RA none;
RT "Genome sequence of the nematode C. elegans: A platform for
investigating biology."
RL Science 282:2012-2018(1998).
DR EMBL: AL161712; CAC70134.1; -.
DR InterPro: IPR000822; Znf_C2H2.
DR Pfam: PF00096; Zf-C2H2_2.
DR SMART: SM00355; Znf_C2H2_3.
DR PROSITE: PS00028; ZINC_FINGER_C2H2_1; UNKNOWN_2.
DR PROSITE: PS0157; ZINC_FINGER_C2H2_2; 1.
KW DNA-binding; Zinc-finger.
SQ SEQUENCE 343 AA; 37946 MW; E91FA2FB5E72A210 CRC64;

Query Match 3.3%; Score 10; DB 5; Length 343;
Best Local Similarity 100.0%; Pred. No. 0.31;
Matches 10; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 157 TFSASSSSSSE 166
|||||

DB 202 TFSASSSSE 211

RESULT 2

ID 091443 PRELIMINARY; PRT: 327 AA.

AC 091443;

DT 01-MAR-2001 (TREMBLrel. 16, Created)

DT 01-MAR-2001 (TREMBLrel. 16, last sequence update)

DT 01-OCT-2001 (TREMBLrel. 18, last annotation update)

DE Probable transmembrane sensor.

GN PAL301.

OS Pseudomonas aeruginosa.

OC Bacteria; Proteobacteria; gamma subdivision; Pseudomonadaceae;

OC Pseudomonas.

OX NCBI_TaxID=287;

RN [1]

RP SEQUENCE FROM N.A.

RC STRAIN=ATCC 15692 / PA01;

RA MEDLINE=20437337; PubMed=10984043;

RA Stoyer C.K., Pham X.-Q.T., Erwin A.L., Mizoguchi S.D., Warren P.,

RA Hickey M.J., Brinkman F.S.L., Hufnagle W.O., Kowalik D.J., Lagrou M.,

RA Garber R.L., Goltz L., Tolentino E., Westbrook-Wadman S., Yan Y.,

RA Brody L.L., Coulter S.N., Folger K.R., Kas A., Lardig K., Lim R.M.,

RA Smith K.A., Spencer D.H., Wong G.K.-S., Wu Z., Paulsen I.T.,

RA Reizer J., Sailer M.H., Hancock R.E.W., Lory S., Olson M.V.,

RT *Complete genome sequence of Pseudomonas aeruginosa PA01, an

RT opportunistic pathogen.";

RT Nature 406:959-964 (2000).

RL EMBL: AF004559; AAC04690.1; -

DR Transmembrane; Complete proteome.

SK SEQUENCE 327 AA; 36641 MW; F4DE4A731326F23E CRC64;

QY Query Match 3.0%; Score 9; DB 16; Length 327;

Best Local Similarity 100.0%; Pred. No. 2.8;

Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

DB 304 LALPALPV 312

QY 16 LALPALPV 24

DB 304 LALPALPV 312

RESULT 3

Q9SH82 PRELIMINARY; PRT: 561 AA.

AC Q9SH82;

DT 01-MAY-2000 (TREMBLrel. 13, Created)

DT 01-MAY-2000 (TREMBLrel. 13, last sequence update)

DT 01-MAR-2002 (TREMBLrel. 20, last annotation update)

DE Putative Na+-dependent inorganic phosphate cotransporter.

GN AT2638060.

OS Arabidopsis thaliana (Mouse-ear cress).

OC Eukaryota; Viridiplantae; Streptophyta; Embryophyta; Tracheophyta;

OC Spermatophyta; Magnoliophyta; eudicotyledons; core eudicots; Rosidae;

OC eurosids II; Brassicales; Brassicaceae; Arabidopsis.

OX NCBI_TaxID=3702;

RN [1]

RP SEQUENCE FROM N.A.

RC STRAIN=CV. COLUMBIA;

RA MEDLINE=20083487; PubMed=10617197;

RA Lin X., Kaul S., Rounsley S.D., Shea T.P., Benito M.-I., Town C.D.,

RA Fujii C.Y., Mason T.M., Bowman C.L., Barnstead M.E., Feldblum T.V.,

RA Buell C.R., Ketchum K.A., Lee J.J., Ronning C.M., Koo H., Moffat K.S.,

RA Cronin L.A., Shen M., VanAken S.E., Unayam L., Tallon L.J., Gill J.E.,

RA Adams M.D., Carrera A.J., Creasy T.H., Goodman H.M., Somerville C.R.,

RA Copenhaver G.P., Preuss D., Niernman W.C., White O., Eisen J.A.,

RA Salzberg S.L., Fraser C.M., Venter J.C.;

RT *Sequence and analysis of chromosome 2 of the plant Arabidopsis

RT thaliana.";

RL Nature 402:761-768 (1999).

RN [2]

RP SEQUENCE FROM N.A.

RC STRAIN=CV. COLUMBIA;

RA Lin X.;

RL Submitted (MAR-2000) to the EMBL/Genbank/DBJ databases.

CC -1- SUBCELLULAR LOCATION: INTEGRAL MEMBRANE PROTEIN (BY SIMILARITY).

DR EMBL: AC007661; AAD32766.1; -

DR InterPro: IPR003662; sub_transporter.

DR Pfam: PF00083; sugar_tr.1.

DR Transmembrane.

SK SEQUENCE 561 AA; 61232 MW; EEPB0BF3127E7680 CRC64;

QY Query Match 3.0%; Score 9; DB 10; Length 561;

Best Local Similarity 100.0%; Pred. No. 4.7;

Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

DB 405 GPGSLTCL 413

QY 6 GPGSLTCL 14

DB 405 GPGSLTCL 413

RESULT 4

ID 089888 PRELIMINARY; PRT: 54 AA.

AC 089888;

DT 01-NOV-1998 (TREMBLrel. 08, Created)

DT 01-NOV-1998 (TREMBLrel. 08, last sequence update)

DT 01-DEC-2001 (TREMBLrel. 19, last annotation update)

DE Large T and small t antigens (Fragment).

OS Budgetigar fledgling disease virus (BFDV).

OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.

OX NCBI_TaxID=10625;

RN [1]

RP SEQUENCE FROM N.A.

RC STRAIN=MCFL97;

RA Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.;

RT *Genetic Diversity In 20 Variants of the Avian Polyomavirus.";

RL Submitted (MAR-1998) to the EMBL/Genbank/DBJ databases.

DR EMBL: AF054402; AAC33626.1; -

DR InterPro: IPR001623; DnaJ_N.

DR Pfam: PF00226; DnaJ.1.

DR SMART: SM00271; DnaJ.1.

DR PROSITE: PS50076; DnaJ_2; 1.

FT NON_TER 54

FT 54

SO SEQUENCE 54 AA; 6077 MW; 5AF094925DEBC997 CRC64;

QY Query Match 2.7%; Score 8; DB 12; Length 54;

Best Local Similarity 100.0%; Pred. No. 5.1;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

DB 259 RRTTELG 266

QY 5 RRTTELG 12

DB 5 RRTTELG 12

RESULT 5

ID 089889 PRELIMINARY; PRT: 54 AA.

AC 089889;

DT 01-NOV-1998 (TREMBLrel. 08, Created)

DT 01-NOV-1998 (TREMBLrel. 08, last sequence update)

DT 01-JUN-2001 (TREMBLrel. 17, last annotation update)

DE Large T and small t antigens (Fragment).

OS Budgetigar fledgling disease virus (BFDV).

OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.

OX NCBI_TaxID=10625;

RN [1]

RP SEQUENCE FROM N.A.

RC STRAIN=DM192;

RA Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.;

RT *Genetic Diversity In 20 Variants of the Avian Polyomavirus.";

RL Submitted (MAR-1998) to the EMBL/Genbank/DBJ databases.

DR EMBL: AF054403; AAC33627.1; -

DR InterPro: IPR001623; DnaJ_N.

DR Pfam: PF00226; DnaJ.1.

DR SMART: SM00271; DnaJ.1.

DR PROSITE: PSS0076; DNAS_2; 1.
FT NON_TER 54
SQ SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;
Query Match
Best Local Similarity 100.0%; Score 8; DB 12; Length 54;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 259 RRLTELLG 266
Db 5 RRLTELLG 12

RESULT 6
089890 PRELIMINARY; PRT; 54 AA.
ID 089890;
AC 089890;
DT 01-NOV-1998 (TREMBlrel. 08, Created)
DT 01-NOV-1998 (TREMBlrel. 08, Last sequence update)
DT 01-JUN-2001 (TREMBlrel. 17, Last annotation update)
DE Large T and small t antigens (Fragment).
OS Budgerigar fledgling disease virus (BFDV).
OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.
RN NCBI_TaxID=10625;
RP SEQUENCE FROM N.A.
RC Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.;
RT "Genetic Diversity in 20 Variants of the Avian Polyomavirus.";
RL Submitted (MAR-1998) to the EMBL/GenBank/DBJ databases.
DR EMBL: AF054404; AAC33628.1;
DR InterPro: IPR001623; DnaJ_N.
DR Pfam: PF00226; DnaJ_1.
DR SMART: SM00271; DnaJ_1.
DR PROSITE: PSS0076; DNAS_2; 1.
FT NON_TER 54
SQ SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;

Query Match
Best Local Similarity 100.0%; Score 8; DB 12; Length 54;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 259 RRLTELLG 266
Db 5 RRLTELLG 12

RESULT 7
089891 PRELIMINARY; PRT; 54 AA.
ID 089891;
AC 089891;
DT 01-NOV-1998 (TREMBlrel. 08, Created)
DT 01-NOV-1998 (TREMBlrel. 08, Last sequence update)
DT 01-JUN-2001 (TREMBlrel. 17, Last annotation update)
DE Large T and small t antigens (Fragment).
OS Budgerigar fledgling disease virus (BFDV).
OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.
RN NCBI_TaxID=10625;
RP SEQUENCE FROM N.A.
RC Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.;
RT "Genetic Diversity in 20 Variants of the Avian Polyomavirus.";
RL Submitted (MAR-1998) to the EMBL/GenBank/DBJ databases.
DR EMBL: AF054405; AAC33629.1;
DR InterPro: IPR001623; DnaJ_N.
DR Pfam: PF00226; DnaJ_1.
DR SMART: SM00271; DnaJ_1.
DR PROSITE: PSS0076; DNAS_2; 1.
FT NON_TER 54
SQ SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;

Query Match
Best Local Similarity 100.0%; Score 8; DB 12; Length 54;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Best Local Similarity 100.0%; Pred. No. 5.1;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 259 RRLTELLG 266
Db 5 RRLTELLG 12

RESULT 8
089892 PRELIMINARY; PRT; 54 AA.
ID 089892;
AC 089892;
DT 01-NOV-1998 (TREMBlrel. 08, Created)
DT 01-NOV-1998 (TREMBlrel. 08, Last sequence update)
DT 01-JUN-2001 (TREMBlrel. 17, Last annotation update)
DE Large T and small t antigens (Fragment).
OS Budgerigar fledgling disease virus (BFDV).
OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.
RN NCBI_TaxID=10625;
RP SEQUENCE FROM N.A.
RC Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.;
RT "Genetic Diversity in 20 Variants of the Avian Polyomavirus.";
RL Submitted (MAR-1998) to the EMBL/GenBank/DBJ databases.
DR EMBL: AF054406; AAC33630.1;
DR InterPro: IPR001623; DnaJ_N.
DR Pfam: PF00226; DnaJ_1.
DR SMART: SM00271; DnaJ_1.
DR PROSITE: PSS0076; DNAS_2; 1.
FT NON_TER 54
SQ SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;

Query Match
Best Local Similarity 100.0%; Score 8; DB 12; Length 54;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 259 RRLTELLG 266
Db 5 RRLTELLG 12

RESULT 9
089893 PRELIMINARY; PRT; 54 AA.
ID 089893;
AC 089893;
DT 01-NOV-1998 (TREMBlrel. 08, Created)
DT 01-NOV-1998 (TREMBlrel. 08, Last sequence update)
DT 01-JUN-2001 (TREMBlrel. 17, Last annotation update)
DE Large T and small t antigens (Fragment).
OS Budgerigar fledgling disease virus (BFDV).
OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.
RN NCBI_TaxID=10625;
RP SEQUENCE FROM N.A.
RC Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.;
RT "Genetic Diversity in 20 Variants of the Avian Polyomavirus.";
RL Submitted (MAR-1998) to the EMBL/GenBank/DBJ databases.
DR EMBL: AF054407; AAC33631.1;
DR InterPro: IPR001623; DnaJ_N.
DR Pfam: PF00226; DnaJ_1.
DR SMART: SM00271; DnaJ_1.
DR PROSITE: PSS0076; DNAS_2; 1.
FT NON_TER 54
SQ SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;

Query Match
Best Local Similarity 100.0%; Score 8; DB 12; Length 54;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 259 RRLTELLG 266
Db 5 RRLTELLG 12

DB 5 RRTTELG 12

RESULT 10

089894 PRELIMINARY; PRT; 54 AA.

ID 089894

AC 089894

DT 01-NOV-1998 (TREMBLrel. 08, Created)

DT 01-NOV-1998 (TREMBLrel. 08, last sequence update)

DT 01-JUN-2001 (TREMBLrel. 17, last annotation update)

DE Large T and small t antigens (Fragment).

OS Budgerigar fledgling disease virus (BFDV).

OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.

OX NCBI_TaxID=10625;

RN [1]

RP SEQUENCE FROM N.A.

RC STRAIN-BD1889;

RA Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.; "Genetic Diversity in 20 Variants of the Avian Polyomavirus.";

RT Submitted (MAR-1998) to the EMBL/Genbank/DBJ databases.

DR EMBL; AF054408; AAC33632.1; -

DR InterPro: IPR001623; DnaJ_N.

DR Pfam: PF00226; DnaJ_1.

DR SMART; SM00271; DnaJ_1.

DR PROSITE; PS50076; DnaJ_2; 1.

FT NON_TER 54

FT SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;

Query Match 2.7%; Score 8; DB 12; Length 54;
Best Local Similarity 100.0%; Pred. No. 5.1;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 259 RRTTELG 266

DB 5 RRTTELG 12

RESULT 11

089895 PRELIMINARY; PRT; 54 AA.

ID 089895

AC 089895

DT 01-NOV-1998 (TREMBLrel. 08, Created)

DT 01-NOV-1998 (TREMBLrel. 08, last sequence update)

DT 01-JUN-2001 (TREMBLrel. 17, last annotation update)

DE Large T and small t antigens (Fragment).

OS Budgerigar fledgling disease virus (BFDV).

OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.

OX NCBI_TaxID=10625;

RN [1]

RP SEQUENCE FROM N.A.

RC STRAIN-BD1889;

RA Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.; "Genetic Diversity in 20 Variants of the Avian Polyomavirus.";

RT Submitted (MAR-1998) to the EMBL/Genbank/DBJ databases.

DR EMBL; AF054409; AAC33633.1; -

DR InterPro: IPR001623; DnaJ_N.

DR Pfam; PF00226; DnaJ_1.

DR SMART; SM00271; DnaJ_1.

DR PROSITE; PS50076; DnaJ_2; 1.

FT NON_TER 54

FT SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;

Query Match 2.7%; Score 8; DB 12; Length 54;
Best Local Similarity 100.0%; Pred. No. 5.1;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 259 RRTTELG 266

DB 5 RRTTELG 12

RESULT 12

089897

ID 089897 PRELIMINARY; PRT; 54 AA.

AC 089897

DT 01-NOV-1998 (TREMBLrel. 08, Created)

DT 01-NOV-1998 (TREMBLrel. 08, last sequence update)

DT 01-JUN-2001 (TREMBLrel. 17, last annotation update)

DE Large T and small t antigens (Fragment).

OS Budgerigar fledgling disease virus (BFDV).

OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.

OX NCBI_TaxID=10625;

RN [1]

RP SEQUENCE FROM N.A.

RC STRAIN-BD1889;

RA Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.; "Genetic Diversity in 20 Variants of the Avian Polyomavirus.";

RT Submitted (MAR-1998) to the EMBL/Genbank/DBJ databases.

DR EMBL; AF054411; AAC33635.1; -

DR InterPro: IPR001623; DnaJ_N.

DR Pfam; PF00226; DnaJ_1.

DR SMART; SM00271; DnaJ_1.

DR PROSITE; PS50076; DnaJ_2; 1.

FT NON_TER 54

FT SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;

Query Match 2.7%; Score 8; DB 12; Length 54;
Best Local Similarity 100.0%; Pred. No. 5.1;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 259 RRTTELG 266

DB 5 RRTTELG 12

RESULT 13

089898 PRELIMINARY; PRT; 54 AA.

ID 089898

AC 089898

DT 01-NOV-1998 (TREMBLrel. 08, Created)

DT 01-NOV-1998 (TREMBLrel. 08, last sequence update)

DT 01-JUN-2001 (TREMBLrel. 17, last annotation update)

DE Large T and small t antigens (Fragment).

OS Budgerigar fledgling disease virus (BFDV).

OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.

OX NCBI_TaxID=10625;

RN [1]

RP SEQUENCE FROM N.A.

RC STRAIN-BDGA81-A;

RA Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.; "Genetic Diversity in 20 Variants of the Avian Polyomavirus.";

RT Submitted (MAR-1998) to the EMBL/Genbank/DBJ databases.

DR EMBL; AF054412; AAC33636.1; -

DR InterPro: IPR001623; DnaJ_N.

DR Pfam; PF00226; DnaJ_1.

DR SMART; SM00271; DnaJ_1.

DR PROSITE; PS50076; DnaJ_2; 1.

FT NON_TER 54

FT SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;

Query Match 2.7%; Score 8; DB 12; Length 54;
Best Local Similarity 100.0%; Pred. No. 5.1;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 259 RRTTELG 266

DB 5 RRTTELG 12

RESULT 14

089899 PRELIMINARY; PRT; 54 AA.

ID 089899

AC 089899

DT 01-NOV-1998 (TREMBLrel. 08, Created)

DT 01-NOV-1998 (TREMBLrel. 08, last sequence update)

DT 01-JUN-2001 (TREMBLrel. 17, last annotation update)

DE Large T and small t antigens (Fragment).
 OS Budderigar fledgling disease virus (BFDV).
 OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.
 OX NCBI_TaxID=10625;

RN [1]
 RP SEQUENCE FROM N.A.

RC STRAIN-BDGA81-B;

RA Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.;

RT "Genetic Diversity in 20 Variants of the Avian Polyomavirus.";

RL Submitted (MAR-1998) to the EMBL/GenBank/DBJ databases.

DR EMBL; AF054413; AAC33637.1; -

DR InterPro: IPR001623; DnaJ_N.

DR Pfam: PF00226; DnaJ; 1.

DR SMART: SM00271; DnaJ; 1.

DR PROSITE: PSS0076; DnaJ_2; 1.

FT NON_TER 54

SO SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;

Query Match 2.7%; Score 8; DB 12; Length 54;

Best Local Similarity 100.0%; Pred. No. 5.1;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 259 RRLTELLG 266

DB 5 RRLTELLG 12

RESULT 15

ID 089900 PRELIMINARY; PRT; 54 AA.

AC 089900;

DT 01-NOV-1998 (TREMUREL.08, Created)

DT 01-NOV-1998 (TREMUREL.08, Last sequence update)

DT 01-JUN-2001 (TREMUREL.17, Last annotation update)

DE Large T and small t antigens (Fragment).

OS Budderigar fledgling disease virus (BFDV).

OC Viruses; dsDNA viruses, no RNA stage; Polyomaviridae; Polyomavirus.

OX NCBI_TaxID=10625;

RN [1]

RP SEQUENCE FROM N.A.

RC STRAIN-BCFL92;

RA Phalen D.N., Wilson V.G., Gaskin J.M., Derr J.N., Graham D.L.;

RT "Genetic Diversity in 20 Variants of the Avian Polyomavirus.";

RL Submitted (MAR-1998) to the EMBL/GenBank/DBJ databases.

DR EMBL; AF054414; AAC33638.1; -

DR InterPro: IPR001623; DnaJ_N.

DR Pfam: PF00226; DnaJ; 1.

DR SMART: SM00271; DnaJ; 1.

DR PROSITE: PSS0076; DnaJ_2; 1.

FT NON_TER 54

SO SEQUENCE 54 AA; 6077 MW; 5AF094925DE8C997 CRC64;

Query Match 2.7%; Score 8; DB 12; Length 54;

Best Local Similarity 100.0%; Pred. No. 5.1;

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 259 RRLTELLG 266

DB 5 RRLTELLG 12

Search completed: July 16, 2003, 19:41:59

Job time : 35 secs

GenCore version 5.1.6
Copyright (c) 1993 - 2003 CompuGen Ltd.

OM protein - protein search, using sw model

Run on: July 16, 2003, 19:25:33 ; Search time 38 Seconds

(without alignments)
1051.979 Million cell updates/sec

Title: US-09-935-727-2

Perfect score: 1634

Sequence: 1 MRALEGPGLSLCLVLAIPA.....RVARMGRLERSVREPLPVH 300

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 908470

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database : A.Geneseq.101002:*

- 1: /SID2/gcgdata/geneseq/geneseq-emb1/AA1980.DAT:*
- 2: /SID2/gcgdata/geneseq/geneseq-emb1/AA1981.DAT:*
- 3: /SID2/gcgdata/geneseq/geneseq-emb1/AA1982.DAT:*
- 4: /SID2/gcgdata/geneseq/geneseq-emb1/AA1983.DAT:*
- 5: /SID2/gcgdata/geneseq/geneseq-emb1/AA1984.DAT:*
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- 7: /SID2/gcgdata/geneseq/geneseq-emb1/AA1986.DAT:*
- 8: /SID2/gcgdata/geneseq/geneseq-emb1/AA1987.DAT:*
- 9: /SID2/gcgdata/geneseq/geneseq-emb1/AA1988.DAT:*
- 10: /SID2/gcgdata/geneseq/geneseq-emb1/AA1989.DAT:*
- 11: /SID2/gcgdata/geneseq/geneseq-emb1/AA1990.DAT:*
- 12: /SID2/gcgdata/geneseq/geneseq-emb1/AA1991.DAT:*
- 13: /SID2/gcgdata/geneseq/geneseq-emb1/AA1992.DAT:*
- 14: /SID2/gcgdata/geneseq/geneseq-emb1/AA1993.DAT:*
- 15: /SID2/gcgdata/geneseq/geneseq-emb1/AA1994.DAT:*
- 16: /SID2/gcgdata/geneseq/geneseq-emb1/AA1995.DAT:*
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- 18: /SID2/gcgdata/geneseq/geneseq-emb1/AA1997.DAT:*
- 19: /SID2/gcgdata/geneseq/geneseq-emb1/AA1998.DAT:*
- 20: /SID2/gcgdata/geneseq/geneseq-emb1/AA1999.DAT:*
- 21: /SID2/gcgdata/geneseq/geneseq-emb1/AA2000.DAT:*
- 22: /SID2/gcgdata/geneseq/geneseq-emb1/AA2001.DAT:*
- 23: /SID2/gcgdata/geneseq/geneseq-emb1/AA2002.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | Query Match | Length | DB ID | Description |
|------------|-------|-------------|--------|-------|-------------|
| 1 | 1634 | 100.0 | 300 | 19 | AAW66102 |
| 2 | 1634 | 100.0 | 300 | 19 | AAW63622 |
| 3 | 1634 | 100.0 | 300 | 20 | AAV03099 |
| 4 | 1634 | 100.0 | 300 | 20 | AAV42182 |
| 5 | 1634 | 100.0 | 300 | 20 | AAV17479 |
| 6 | 1634 | 100.0 | 300 | 20 | AAV06817 |
| 7 | 1634 | 100.0 | 300 | 20 | AAW97749 |
| 8 | 1634 | 100.0 | 300 | 20 | AAW95082 |
| 9 | 1634 | 100.0 | 300 | 21 | AAH19335 |
| 10 | 1634 | 100.0 | 300 | 21 | AAW28559 |

| | | | | | |
|----|------|-------|-----|----|----------|
| 11 | 1634 | 100.0 | 300 | 21 | AAW24057 |
| 12 | 1634 | 100.0 | 300 | 21 | AAW33416 |
| 13 | 1634 | 100.0 | 300 | 21 | AAW03621 |
| 14 | 1634 | 100.0 | 300 | 21 | AAV97246 |
| 15 | 1634 | 100.0 | 300 | 21 | AAV90357 |
| 16 | 1634 | 100.0 | 300 | 21 | AAW24395 |
| 17 | 1634 | 100.0 | 300 | 21 | AAV96596 |
| 18 | 1634 | 100.0 | 300 | 22 | AAE03568 |
| 19 | 1634 | 100.0 | 300 | 22 | AAW74466 |
| 20 | 1634 | 100.0 | 300 | 22 | AAW71754 |
| 21 | 1634 | 100.0 | 300 | 22 | AAW48161 |
| 22 | 1634 | 100.0 | 300 | 22 | AAW50903 |
| 23 | 1634 | 100.0 | 300 | 23 | AAE14579 |
| 24 | 1634 | 100.0 | 300 | 23 | AAE20848 |
| 25 | 1634 | 100.0 | 341 | 22 | AAW73740 |
| 26 | 1620 | 99.1 | 300 | 21 | AAV77458 |
| 27 | 1619 | 99.1 | 300 | 21 | AAW19710 |
| 28 | 1619 | 99.1 | 300 | 21 | AAV96597 |
| 29 | 1619 | 99.1 | 300 | 22 | AAE03570 |
| 30 | 1619 | 99.1 | 300 | 22 | AAW83950 |
| 31 | 1619 | 99.1 | 300 | 22 | AAW68045 |
| 32 | 1619 | 99.1 | 300 | 22 | AAW68048 |
| 33 | 1619 | 99.1 | 300 | 23 | AAE14580 |
| 34 | 1610 | 98.5 | 302 | 20 | AAV42183 |
| 35 | 1532 | 93.8 | 326 | 23 | ABP41980 |
| 36 | 1509 | 92.4 | 300 | 21 | AAW03623 |
| 37 | 1502 | 91.9 | 300 | 21 | AAW03622 |
| 38 | 1502 | 91.9 | 300 | 21 | AAW03624 |
| 39 | 1491 | 91.2 | 271 | 20 | AAV42184 |
| 40 | 1491 | 91.2 | 271 | 21 | AAW19334 |
| 41 | 1491 | 91.2 | 271 | 21 | AAW19705 |
| 42 | 1491 | 91.2 | 271 | 21 | AAV97247 |
| 43 | 1481 | 91.2 | 271 | 21 | AAV96598 |
| 44 | 1481 | 91.2 | 271 | 22 | AAE03567 |
| 45 | 1491 | 91.2 | 271 | 22 | AAW68044 |

ALIGNMENTS

| | | |
|----------|--|----------------------------|
| RESULT 1 | AAW66102 | standard; Protein; 300 AA. |
| ID | AAW66102 | |
| XX | AAW66102: | |
| XX | 02-DEC-1998 (first entry) | |
| DT | 02-DEC-1998 | |
| DE | Amino acid sequence of tumour necrosis related receptor (TR4). | |
| KW | Human; tumour necrosis related receptor; TR4; agonist; antagonist; | |
| KW | inhibition; chronic; acute; inflammation; arthritis; septicaemia; | |
| KW | autoimmune disease; transplant rejection; stroke; cancer; | |
| KW | Alzheimer's disease. | |
| XX | | |
| OS | Homo sapiens. | |
| XX | | |
| PN | EP861850-A1. | |
| XX | | |
| PD | 02-SEP-1998. | |
| XX | | |
| PF | 20-JAN-1998: 98BP-0300382. | |
| XX | | |
| PR | 04-FEB-1997: 97US-0794796. | |
| XX | | |
| PA | (SMK) SMITHKLINE BECHAM CORP. | |
| XX | | |
| PI | Emery J, Tan KB, Truneh A, Young PR; | |
| DR | WPI, 1998-508248/44. | |
| DR | N-PSDB: AAV07654. | |
| XX | | |
| PT | New DNA encoding tumour necrosis related receptor - used to treat | |

Human PRO212 prote
Human PRO212 prote
Human Fas ligand i
M68 TNF receptor r
Human tumour necro
Human PRO212 prote
Human FLINT. Homo
Human native fas i
Human FLINT native
Human NTR3. Homo
Human PRO212 polyp
Human PRO212 prote
Human native FLINT
Human tumour necro
Human colon cancer
Human TNF receptor
Human Fas ligand i
Human FLINT. Homo
Human fas ligand i
Amino acid sequenc
Amino acid sequenc
Amino acid sequenc
Human FLINT analog
Human FLINT #2 pro
Human ovarian anti
Human Fas ligand i
Monkey Fas ligand i
Human Fas ligand i
Human mFLINT #1 pr
A mature human FAS
Human FAS ligand i
M68 TNF receptor r
Human mature FLINT
Human mature fas i
Amino acid sequenc

PT and prevent e.g. inflammation, arthritis, septicaemia, autoimmune
PT diseases, transplant rejection, infection, stroke, ischaemia, AIDS,
PS restenosis, AIDS, bone disorders and cancer

Claim 1; Fig 1; 21pp; English.

CC This is the amino acid sequence of the human tumour necrosis related
CC receptor (TR4), used in the method of the invention. The TR4 protein
CC or its agonist can be used to treat a subject in need of enhanced
CC TR4 polypeptide activity. The antagonist is used to inhibit TR4
CC polypeptide activity. The active agents can be used for the
CC treatment and prevention of diseases such as chronic and acute
CC inflammation, arthritis, septicaemia, autoimmune diseases, transplant
CC rejection, stroke, cancer, Alzheimer's disease.

CC Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 19; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.4e-121;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 MRALEGPGLSLICLVLPALLPVPVAVGVAETPTYPWRDAETGERLVCACCPGTFVQR 60

DB 1 MRALEGPGLSLICLVLPALLPVPVAVGVAETPTYPWRDAETGERLVCACCPGTFVQR 60

OY 61 PCRRDSPPTGCPCPRRHTQFWNVLERCRCNVLCGEEREERARACHATHNACRCRTGFF 120

DB 61 PCRRDSPPTGCPCPRRHTQFWNVLERCRCNVLCGEEREERARACHATHNACRCRTGFF 120

OY 121 AHAGFCLFHASCPCPGAGVIATGTPSONTOCCPCPGTSSASSSSSECCQPHRNCATGLA 180

DB 121 AHAGFCLFHASCPCPGAGVIATGTPSONTOCCPCPGTSSASSSSSECCQPHRNCATGLA 180

OY 181 LNVPGSSSHDPLCTSGTFPLSTRVPAEBCERAVIDFVAFODISIKRLQRLQALEAPE 240

DB 181 LNVPGSSSHDPLCTSGTFPLSTRVPAEBCERAVIDFVAFODISIKRLQRLQALEAPE 240

OY 241 GMGPTPRAGRAALQKLRRLTELLGADGALLVRLQALVARNPGLERSVREFFLVH 300

DB 241 GMGPTPRAGRAALQKLRRLTELLGADGALLVRLQALVARNPGLERSVREFFLVH 300

RESULT 2

AAW63622
ID AAW63622 standard; Protein: 300 AA.

AC AAW63622;

DT 26-OCT-1998 (first entry)

XX Human tumour necrosis factor receptor-6 alpha protein.

KW Human tumour necrosis factor receptor-6 alpha; TNFR-6 alpha; TNFR-6 beta;
KW endothelial cells; keratinocytes; normal prostate; apoptosis;

KW prostate tumour tissue.

OS Homo sapiens.

XX Key Location/Qualifiers

FT Peptide 1..30

FT Protein 31..300

FT Region /note="TNFR-6 alpha"

XX MO9830694-A2.

XX 16-JUL-1998.

XX 13-JAN-1998; 98WO-US00153.

XX 14-JAN-1997; 97US-0035496.

PA (HUMA-) HUMAN GENOME SCI INC.

XX Ebner R, Feng P, Gentz RL, Ni J, Ruben SM, Yu G;

XX WPI: 1998-399142/34.

DR N-PSDB: AAV39085.

PT Human tumour necrosis factor receptors 6-alpha and 6-beta - used in
PT the diagnosis of immune system-related disorder(s)

Claim 20; Fig 1; 91pp; English.

CC The present sequence represents the human tumour necrosis factor
CC receptor-6 alpha (TNFR-6 alpha) protein. The invention also provides
CC for the TNFR-6 beta protein (AAW63623). TNFR-6 alpha and TNFR-6 beta
CC are members of the tumour necrosis factor receptor (TNFR) family. TNFRs
CC are expressed in endothelial cells, keratinocytes, normal prostate and
CC prostate tumour tissue. For a number of disorders of these cells,
CC particularly of the immune system, substantially altered (whether
CC increased or decreased) levels of TNFR-6 alpha and/or TNFR-6 beta
CC expression can be detected, therefore the TNFR-6 alpha and TNFR-6 beta
CC polypeptides, nucleic acids and antibodies are claimed to be useful in
CC the diagnosis of such disorders. Mutations of the TNFR-6 alpha and
CC TNFR-6 beta genes can also be detected. The TNFR polypeptides are
CC also claimed to be useful for identifying ligands which may be useful
CC in the treatment of apoptosis related disorders.

CC Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 19; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.4e-121;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 MRALEGPGLSLICLVLPALLPVPVAVGVAETPTYPWRDAETGERLVCACCPGTFVQR 60

DB 1 MRALEGPGLSLICLVLPALLPVPVAVGVAETPTYPWRDAETGERLVCACCPGTFVQR 60

OY 61 PCRRDSPPTGCPCPRRHTQFWNVLERCRCNVLCGEEREERARACHATHNACRCRTGFF 120

DB 61 PCRRDSPPTGCPCPRRHTQFWNVLERCRCNVLCGEEREERARACHATHNACRCRTGFF 120

OY 121 AHAGFCLFHASCPCPGAGVIATGTPSONTOCCPCPGTSSASSSSSECCQPHRNCATGLA 180

DB 121 AHAGFCLFHASCPCPGAGVIATGTPSONTOCCPCPGTSSASSSSSECCQPHRNCATGLA 180

OY 181 LNVPGSSSHDPLCTSGTFPLSTRVPAEBCERAVIDFVAFODISIKRLQRLQALEAPE 240

DB 181 LNVPGSSSHDPLCTSGTFPLSTRVPAEBCERAVIDFVAFODISIKRLQRLQALEAPE 240

OY 241 GMGPTPRAGRAALQKLRRLTELLGADGALLVRLQALVARNPGLERSVREFFLVH 300

DB 241 GMGPTPRAGRAALQKLRRLTELLGADGALLVRLQALVARNPGLERSVREFFLVH 300

RESULT 3

AAV03099
ID AAV03099 standard; Protein: 300 AA.

AC AAV03099;

DT 09-DEC-1999 (first entry)

XX Human lung TNF-receptor protein.

KW Tumour necrosis factor; TNF; TNF receptor; human; lung; gene therapy;
KW detection; immunoassay; diagnosis; disease; immune system; tumour;

KW osteogenic system; cardiovascular system; central nervous system; asthma;
KW peripheral nervous systems; transplant incompatibility; antitumor;

KW rheumatoid arthritis; antiasthmatic; antiarthritic.

OS Homo sapiens.

XX Key Location/Qualifiers


```

FT CDS 134..1036
FT /*tag= a
FT /product= "TNF-receptor"
XX
XX DEL9809978-A1.
XX
XX 16-SEP-1999.
XX
XX 09-MAR-1998; 98DE-1009978.
XX
XX 09-MAR-1998; 98DE-1009978.
XX
XX (BADI ) BASF AG.
XX
XX Kroeger B;
XX
XX WPI; 1999-519473/44.
XX
XX N-PSDB; AAZ09998.
XX
XX New soluble member of tumor necrosis factor receptor family, useful for
XX identification specific modulators and for treating disease e.g. tumors
XX
XX
XX Claim 1; Page 8-9; 10pp; German.
XX
XX This invention describes a novel tumour necrosis factor (TNF) receptor
XX (I) isolated from human lung tissue. (I) is used: (i) to raise specific
XX antibodies (Ab); (ii) to screen for specific (ant)agonists or ligands
XX (A), potential therapeutic agents; and (iii) therapeutically (optionally
XX expressed from a gene therapy vector) in conditions associated with a
XX deficit of (I). Ab are used: (a) for qualitative or quantitative
XX detection of (I) in standard immunoassays (for diagnosis of disease, or
XX susceptibility, or for monitoring); and (b) as therapeutic inhibitors in
XX cases where (I) is overexpressed. Nucleic acid (II) that encodes (I) is
XX used: (A) for recombinant production of (I); (B) also its oligonucleotide
XX fragments, in standard hybridization and/or amplification assays; (C) as
XX source of antisense molecules or ribozymes; and (D) to produce transgenic
XX animals (for studying (patho)physiology of (I)). Diseases possibly
XX associated with under- or over-expression of (I) are those of the immune,
XX osteogenic, cardiovascular and central or peripheral nervous systems,
XX tumors, transplant incompatibility, asthma and rheumatoid arthritis. The
XX products of the invention have antitumor, antiasthmatic and
XX antiarthritic activity. This sequence represents the TNF-receptor of the
XX invention.
XX
XX Sequence 300 AA:
XX
XX Query Match 100.0%; Score 1634; DB 20; Length 300;
XX Best Local Similarity 100.0%; Pred. No. 1.4e-121;
XX Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
XX
XX QY 1 MRALBEGFGLSLCLVLPALPVPVAVGVAETPTVWMDAETGERLVCAQCPGGTFVOR 60
XX DB 1 MRALBEGFGLSLCLVLPALPVPVAVGVAETPTVWMDAETGERLVCAQCPGGTFVOR 60
XX QY 61 PCARDSPPTGCPGPPRHYYTFQWYLERCRVCNVLCGRREBARCAHTHRACRCRGGF 120
XX DB 61 PCARDSPPTGCPGPPRHYYTFQWYLERCRVCNVLCGRREBARCAHTHRACRCRGGF 120
XX QY 121 AHAGFCLFHAASCPGAGVIAFGTPTSONTOCCPCPPGTFSSASSSSSECCQPHRNCATAGLA 180
XX DB 121 AHAGFCLFHAASCPGAGVIAFGTPTSONTOCCPCPPGTFSSASSSSSECCQPHRNCATAGLA 180
XX QY 121 AHAGFCLFHAASCPGAGVIAFGTPTSONTOCCPCPPGTFSSASSSSSECCQPHRNCATAGLA 180
XX DB 121 AHAGFCLFHAASCPGAGVIAFGTPTSONTOCCPCPPGTFSSASSSSSECCQPHRNCATAGLA 180
XX QY 181 LNVPGSSSHDTLCTCTGTFPLSTRVPGAECECAVDFVAFODISIKRLORLQALEAPE 240
XX DB 181 LNVPGSSSHDTLCTCTGTFPLSTRVPGAECECAVDFVAFODISIKRLORLQALEAPE 240
XX QY 241 GNGPTPAGRAALQLKRRRLTELLGAQDALLVRLQALRVAMPLESRVERFLPVH 300
XX DB 241 GNGPTPAGRAALQLKRRRLTELLGAQDALLVRLQALRVAMPLESRVERFLPVH 300
XX
XX RESULT 4.

```

```

AAV42182
ID AAV42182 standard; Protein; 300 AA.
XX
XX AC AAV42182;
XX
XX 17-DEC-1999 (first entry)
XX
XX DE Human FLINT #1 protein sequence.
XX
XX KW Human; FLINT; mFLINT; OPG3; tumour necrosis factor receptor; FasL;
XX apoptosis; inflammation; cancer; diabetes; acute liver failure;
XX sepsis; hepatitis; ischaemia-associated injury; hypercoagulation;
XX reperfusion-associated injury; aplastic anaemia; differentiation;
XX growth; myelodysplastic syndrome; pancytopenic condition;
XX myocardial ischaemia.
XX
XX OS Homo sapiens.
XX
XX PN WO950413-A2.
XX
XX PD 07-OCT-1999.
XX
XX PE 30-MAR-1999; 99WO-US06797.
XX
XX PR 30-MAR-1998; 98US-0079856.
XX 20-MAY-1998; 98US-0086074.
XX 09-SEP-1998; 98US-0099643.
XX 17-DEC-1998; 98US-0112577.
XX 18-DEC-1998; 98US-0112703.
XX 18-DEC-1998; 98US-0112933.
XX 22-DEC-1998; 98US-0113407.
XX
XX PA (ELIL ) LILLY & CO ELI.
XX
XX PI Bimol TF, Dou S, Glasbrook AL, Gould KE, Hale JE, Heuer JG;
XX Hui KY, Kharitonov A, Mizrahi J, Na S, Noblitt TW, Reidy CA;
XX Song HY, Wang J, Wu X, Zuckerman SH;
XX
XX DR WPI; 1999-591319/50.
XX N-PSDB; AAZ25375.
XX
XX PT Use of mature FLINT for treating acute liver failure, inflammation,
XX cancer, and diabetes - by prevention of FasL-Fas mediated apoptotic
XX and proinflammatory activity
XX
XX PS Claim 30; Fig 1; 99pp; English.
XX
XX The present invention describes therapeutic applications of mature FLINT
XX (mFLINT) for use in the treatment of acute liver failure. Mature FLINT
XX (mFLINT), which is a member of the tumour necrosis factor receptor
XX superfamily, is used for treating acute liver failure, inflammation of
XX the liver, abnormal hepatocyte apoptosis, sepsis, a disorder associated
XX with inflammation, hepatitis, abnormal apoptosis, an ischaemia-associated
XX injury or disorder such as hypercoagulation (including use with
XX thrombolytic or anti-thrombolytic agents), reperfusion-associated injury
XX or disorder. Type I diabetes, cancer, cell damage or damage to an
XX innocent bystander tissue that is induced by a chemotherapeutic agent or
XX therapeutic irradiation, treating haematopoietic progenitor cells that
XX have been exposed to therapeutic radiation or chemotherapy, aplastic
XX CC anaemia, myelodysplastic syndrome or a pancytopenic condition. mFLINT is
XX also used for promoting the growth or differentiation of a haematopoietic
XX progenitor cell or CD34+ cell and preventing damage to a cardiac myocyte
XX CC resulting from abnormal myocardial ischaemia. The present sequence
XX represents human FLINT.
XX
XX Sequence 300 AA:
XX
XX Query Match 100.0%; Score 1634; DB 20; Length 300;
XX Best Local Similarity 100.0%; Pred. No. 1.4e-121;
XX Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
XX
XX QY 1 MRALBEGFGLSLCLVLPALPVPVAVGVAETPTVWMDAETGERLVCAQCPGGTFVOR 60
XX
XX

```

Db 1 MRALEBPGSLLCVLVIALPALLPVPVAVGVAETPTVPMWDAETGERLVCAQCPPTGVOR 60
 QY 61 PCRDSPTTCGCPPPHHYQFMNMYLERCHYCNVLCGEREEERACHATHNRACRCRTGFF 120
 Db 61 PCRDSPTTCGCPPPHHYQFMNMYLERCHYCNVLCGEREEERACHATHNRACRCRTGFF 120
 QY 121 AHAGFCLHNASCPPGAGVIAFGTPTSONTOCCPCPGTFSASSSSSECCOPHNCTALGIA 180
 Db 121 AHAGFCLHNASCPPGAGVIAFGTPTSONTOCCPCPGTFSASSSSSECCOPHNCTALGIA 180
 QY 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECECERAVIDEVAFODISIKRLORLLQALEAPE 240
 Db 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECECERAVIDEVAFODISIKRLORLLQALEAPE 240
 QY 241 GNGPPTPRAGRAALQKLRRLRTELGAODGALLVRLQLRVARMPLGLERSVREERFLPVH 300
 Db 241 GNGPPTPRAGRAALQKLRRLRTELGAODGALLVRLQLRVARMPLGLERSVREERFLPVH 300

RESULT 5
 AAY17479 standard; Protein: 300 AA.
 ID AAY17479
 AC AAY17479;
 DT 02-AUG-1999 (first entry)
 DE Mammalian tumour necrosis factor receptor OPG-2.
 XX Tumour necrosis factor receptor; TNF receptor; OPG-2; Paget's disease;
 KM osteopenic disorder; osteoclast activity; primary osteoporosis;
 KM hyperglycaemia; osteolytic metastasis; Immune response; cancer.
 XX Mammalia.
 OS
 PN MO9926977-A1.
 PD 03-JUN-1999.
 XX
 PF 24-NOV-1998; 98WO-US25065.
 XX
 PR 17-FEB-1998; 98US-0074896.
 PR 24-NOV-1997; 97US-0066446.
 XX
 PA (BIOI) BIOGEN INC.
 PI
 TS Tschoopp J;
 DR WPI: 1999-347693/29.
 DR N-PSDB: AAX76052.
 XX
 PT New tumour necrosis factor family receptor OPG-2
 XX
 PS Claim 1; Page 18; 22pp; English.
 XX
 CC The present sequence represents a mammalian tumour necrosis factor
 CC receptor, designated OPG-2. OPG-2, is a member of the tumour necrosis
 CC factor receptor family, and can be used: (i) to raise specific
 CC antibodies (Ab), (ii) to treat osteopenic disorders associated with
 CC excessive osteoclast activity, e.g. primary osteoporosis, Paget's
 CC disease, hyperglycaemia of malignancy or osteolytic metastases; (iii)
 CC for affinity purification of cognate ligands, and (iv) to screen for
 CC ligands (antagonists or agonists). Ab, or other OPG-2 blocking agents
 CC such as soluble forms of the protein, are used to prevent, or reduce
 CC severity of, an immune response, and for treating cancer. They can also
 CC be used in diagnostic assays. The nucleic acid sequence encoding OPG-2
 CC can be used as a probe to isolate related sequences from other species.
 XX
 SQ Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 20; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEBPGSLLCVLVIALPALLPVPVAVGVAETPTVPMWDAETGERLVCAQCPPTGVOR 60
 Db 1 MRALEBPGSLLCVLVIALPALLPVPVAVGVAETPTVPMWDAETGERLVCAQCPPTGVOR 60
 QY 61 PCRDSPTTCGCPPPHHYQFMNMYLERCHYCNVLCGEREEERACHATHNRACRCRTGFF 120
 Db 61 PCRDSPTTCGCPPPHHYQFMNMYLERCHYCNVLCGEREEERACHATHNRACRCRTGFF 120
 QY 121 AHAGFCLHNASCPPGAGVIAFGTPTSONTOCCPCPGTFSASSSSSECCOPHNCTALGIA 180
 Db 121 AHAGFCLHNASCPPGAGVIAFGTPTSONTOCCPCPGTFSASSSSSECCOPHNCTALGIA 180
 QY 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECECERAVIDEVAFODISIKRLORLLQALEAPE 240
 Db 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECECERAVIDEVAFODISIKRLORLLQALEAPE 240
 QY 241 GNGPPTPRAGRAALQKLRRLRTELGAODGALLVRLQLRVARMPLGLERSVREERFLPVH 300
 Db 241 GNGPPTPRAGRAALQKLRRLRTELGAODGALLVRLQLRVARMPLGLERSVREERFLPVH 300

RESULT 6
 AAY06817 standard; Protein: 300 AA.
 ID AAY06817
 AC AAY06817;
 DT 24-JUN-1999 (first entry)
 DE Human Dcr3 polypeptide.
 XX Dcr3 polypeptide; tumour necrosis factor receptor; TNFR; Fas ligand;
 KM apoptosis; T cell mediated immune response; allergy; asthma; cancer;
 KM rheumatoid arthritis; Crohn's disease; guest vs. host disease; human;
 KM gene therapy.
 XX
 OS Homo sapiens.
 PN MO9914330-A1.
 PD 25-MAR-1999.
 XX
 PF 18-SEP-1998; 98WO-US19661.
 XX
 PR 30-JUL-1998; 98US-0094640.
 PR 18-SEP-1997; 97US-0059288.
 XX
 PA (GETH) GENENTECH INC.
 PI Ashkenazi AJ, Botstein D, Dodge KH, Goddard A, Gurney AL;
 PI Kim KJ, Lawrence DA, Pitti R, Roy MA, Tumas DB;
 PI Wood WI;
 DR WPI: 1999-244032/20.
 DR N-PSDB: AAX32744.
 XX
 PT Dcr3 polypeptide related to tumor necrosis factor receptor
 XX
 PS Claim 5; Fig 1; 88pp; English.
 XX
 CC This represents a human Dcr3 polypeptide, a homologue of tumour necrosis
 CC factor receptor (TNFR) polypeptide. Host cells containing a vector
 CC comprising the Dcr3 nucleic acid can be used for the recombinant
 CC expression of the protein. Dcr3 binds to Fas ligand, so it (or its
 CC chimeras) are useful for modulating apoptosis in mammalian cells, also
 CC other Fas-ligand induced activities, particularly to inhibit T cell
 CC mediated immune responses, e.g. in treatment of allergy, asthma,
 CC rheumatoid arthritis, Crohn's disease, guest vs. host disease etc. Dcr3
 CC may also be used to identify specific binding proteins, potential
 CC inhibitors. Antibodies against Dcr3 are used to treat cancer.
 CC Specifically of the lung and colon, also in diagnosis and for affinity
 CC purification of the protein. Detecting mutations in the gene for Dcr3 is

CC also used to diagnose cancer, or predisposition to it. Dcr3 nucleic acid
 CC is useful as hybridization probe to detect genomic or related sequences;
 CC for chromosome and gene mapping; as source of antisense sequences; for
 CC expression of recombinant Dcr3 and to generate transgenic animals (for
 CC development and screening of therapeutic agents), also for in vivo or
 CC ex vivo gene therapy.

XX Sequence 300 AA:

Query Match 100.0%; Score 1634; DB 20; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALBPGSLTCLVIALPALLPVPAVRGVAEPPTVPMWDAETGERLVCAQCPRGTFVOR 60
 DB 1 MRALBPGSLTCLVIALPALLPVPAVRGVAEPPTVPMWDAETGERLVCAQCPRGTFVOR 60
 QY 61 PCRDSPTTCGPRPHHTYQFWNYLERCRVCNVLCGEREEARACHATNRCRCRTGTF 120
 DB 61 PCRDSPTTCGPRPHHTYQFWNYLERCRVCNVLCGEREEARACHATNRCRCRTGTF 120
 QY 121 AAAGFLEHASCPCPGAGVIAPTGPTSONTCQPCPGTFSSASSSSSQCPHRCNTALGIA 180
 DB 121 AAAGFLEHASCPCPGAGVIAPTGPTSONTCQPCPGTFSSASSSSSQCPHRCNTALGIA 180
 QY 181 LNVPGSSHDLTCTSGTFPLSTRVPAECERAVIDFAFODISIKRLQRLQALEAPE 240
 DB 181 LNVPGSSHDLTCTSGTFPLSTRVPAECERAVIDFAFODISIKRLQRLQALEAPE 240
 QY 241 GWCPTPRAGRAALQTLKRRRLTELLGAQDGLLVRLQLARVARMGLESYVERELPVH 300
 DB 241 GWCPTPRAGRAALQTLKRRRLTELLGAQDGLLVRLQLARVARMGLESYVERELPVH 300

RESULT 7
 AAM97749
 ID AAM97749 standard; Protein; 300 AA.

XX AAM97749;

XX 21-MAY-1999 (first entry)

XX Human tumour necrosis factor receptor ZTNFR-5.

XX ZTNFR-5: tumour necrosis factor receptor; TNFR; human;

XX cell maturation; bone cell regulation.

XX Homo sapiens.

XX Location/Qualifiers

XX Key 1..23

XX Peptide /note= "signal peptide"

XX Protein 24..300

XX Domain /note= "mature protein"

XX Region 24..194

XX Region 49..71

XX Region /note= "cysteine-rich pseudo-repeat 1"

XX Region 72..113

XX Region /note= "cysteine-rich pseudo-repeat 1"

XX Region 114..151

XX Region /note= "cysteine-rich pseudo-repeat 1"

XX Region 152..194

XX Region /note= "cysteine-rich pseudo-repeat 1"

XX WO9904001-A1.

XX 28-JAN-1999.

XX 21-JUL-1998; 98WO-US15072.

XX 21-JUL-1997; 97US-0053203.

PA (ZYMO) ZYMOGENETICS INC.

XX Farrah TM;

XX WPI; 1999-132245/11.

XX N-PSDB; AAM07226.

XX Novel tumour necrosis factor receptor ZTNFR5 - useful for

XX regulating maturation of TNF-ligand bearing cells

XX Claim 1; Page 84-85; 109pp; English.

CC This polypeptide comprises a new, secreted tumour necrosis factor
 CC receptor (see AAM97749), designated ZTNFR-5. Novel ZTNFR-5 encoding
 CC polynucleotides and polypeptides were initially identified by
 CC querying an expressed sequence tag (EST) database for sequences
 CC homologous to conserved motifs within the TNF receptor family.
 CC Based on this search, a contig of 16 ESTs (see AAX07226) was
 CC constructed. ZTNFR-5 polypeptides comprise 4 cysteine-rich repeats
 CC (see also AAM97750-55) that are homologous to other TNF receptors, in
 CC particular the soluble, secreted TNF receptor osteoprotegerin.
 CC ZTNFR-5 polypeptide can be prepared by recombinant methods. The
 CC polypeptide, especially the extracellular domain, can be used to
 CC generate a soluble variant of ZTNFR-5. The polypeptides and
 CC nucleic acids can be used to screen for ligands, agonists and
 CC antagonists of ZTNFR-5. The polypeptides can be used in bone cell
 CC regulation and to regulate the maturation of TNF ligand-bearing
 CC cells such as T- or B-cells, lymphocytes, peripheral blood
 CC mononuclear cells, polymorphonuclear leukocytes, fibroblasts or
 CC haematopoietic cells.

XX Sequence 300 AA:

Query Match 100.0%; Score 1634; DB 20; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALBPGSLTCLVIALPALLPVPAVRGVAEPPTVPMWDAETGERLVCAQCPRGTFVOR 60
 DB 1 MRALBPGSLTCLVIALPALLPVPAVRGVAEPPTVPMWDAETGERLVCAQCPRGTFVOR 60
 QY 61 PCRDSPTTCGPRPHHTYQFWNYLERCRVCNVLCGEREEARACHATNRCRCRTGTF 120
 DB 61 PCRDSPTTCGPRPHHTYQFWNYLERCRVCNVLCGEREEARACHATNRCRCRTGTF 120
 QY 121 AAAGFLEHASCPCPGAGVIAPTGPTSONTCQPCPGTFSSASSSSSQCPHRCNTALGIA 180
 DB 121 AAAGFLEHASCPCPGAGVIAPTGPTSONTCQPCPGTFSSASSSSSQCPHRCNTALGIA 180
 QY 181 LNVPGSSHDLTCTSGTFPLSTRVPAECERAVIDFAFODISIKRLQRLQALEAPE 240
 DB 181 LNVPGSSHDLTCTSGTFPLSTRVPAECERAVIDFAFODISIKRLQRLQALEAPE 240
 QY 241 GWCPTPRAGRAALQTLKRRRLTELLGAQDGLLVRLQLARVARMGLESYVERELPVH 300
 DB 241 GWCPTPRAGRAALQTLKRRRLTELLGAQDGLLVRLQLARVARMGLESYVERELPVH 300

RESULT 8
 AAM95082
 ID AAM95082 standard; Protein; 300 AA.

XX AAM95082;

XX 20-MAY-1999 (first entry)

XX Orphan receptor (HUMAN NTR-1) polypeptide.

XX HUMAN NTR-1: orphan receptor; osteoprotegerin; OPG; TNFR; human;

XX tumour necrosis factor receptor; muscle disorder; bone mass; screening;

XX muscle metabolism; binding agent; cognate ligand.

XX Homo sapiens.

XX WO9907738-A2.
 PN 18-FEB-1999.
 XX
 PD 04-AUG-1998; 98WO-US16202.
 XX
 PF 06-AUG-1997; 97US-0054869.
 XX
 PR (PROC) PROCTER & GAMBLE CO.
 XX (REGE-) REGENERON PHARM INC.
 PA
 PI Maslakowski PJ, Morris J, Valenzuela DM;
 XX WPI; 1999-167365/14.
 DR N-PSDB; AAX22300.
 XX
 PT Novel orphan human receptor polypeptide and nucleic acid - useful as
 PI diagnostic reagents and for treatment of muscle disorders
 XX
 PS Claim 7, Page 21; 23pp; English.
 XX
 CC This represents a HUMAN NTR-1 polypeptide, a novel orphan receptor. The
 CC protein is related to osteoprotegerin (OPG) and to tumour necrosis factor
 CC receptor (TNFR). Host cells transformed with a vector comprising the
 CC HUMAN NTR-1 nucleic acid are used for the recombinant expression of the
 CC protein. HUMAN NTR-1 proteins and antibodies immune specific for the
 CC protein are useful for diagnosis and treatment of humans and animals,
 CC especially muscle disorders, as the receptor is involved in regulation of
 CC bone mass and muscle metabolism. HUMAN NTR-1 receptors are also useful
 CC for screening for novel binding agents, and cognate ligands, which may be
 CC used to treat disorders associated with HUMAN NTR-1 imbalance.
 CC
 SQ Sequence 300 AA;
 Query Match 100.0%; Score 1634; DB 20; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 1 MRALEGPGLSLCLVLAIPALLPVPVAVGVAVETPTYPMDAETGRLVCAQCPPTGFVOR 60
 DB 1 MRALEGPGLSLCLVLAIPALLPVPVAVGVAVETPTYPMDAETGRLVCAQCPPTGFVOR 60
 QY 61 PCRBDSPPTGCGPPRHHTQFWNYLERCRVCNVLCGERBEERACHAHNRACRRTGFE 120
 DB 61 PCRBDSPPTGCGPPRHHTQFWNYLERCRVCNVLCGERBEERACHAHNRACRRTGFE 120
 QY 121 AHAGFCLHASCPPAGVYIAPETPSONTQCCPCPGTFSASSSSSECCOPHRNCTALGIA 180
 DB 121 AHAGFCLHASCPPAGVYIAPETPSONTQCCPCPGTFSASSSSSECCOPHRNCTALGIA 180
 QY 181 LNVPGSSSHDILCTCTGTFPLSTRVPGAEECEERAVIDFVAFODISIKRLQRLLOALEAPE 240
 DB 181 LNVPGSSSHDILCTCTGTFPLSTRVPGAEECEERAVIDFVAFODISIKRLQRLLOALEAPE 240
 QY 241 GNGPPTPRAGRAALQIKLRRLTELLGADGALLVRLLOALRVARMPGLERSVREFFLPVH 300
 DB 241 GNGPPTPRAGRAALQIKLRRLTELLGADGALLVRLLOALRVARMPGLERSVREFFLPVH 300
 RESULT 9
 AAB19335
 ID AAB19335 standard; Protein; 300 AA.
 AC AAB19335;
 XX
 DT 19-FEB-2001 (first entry)
 XX
 DE A full length human FAS ligand inhibitory Protein (FLINT).
 XX
 KW Human: FAS ligand inhibitory Protein; FLINT; analogue; apoptosis;
 KM tumour necrosis factor receptor; acute lung injury; pulmonary fibrosis;
 KM acute respiratory distress syndrome; ulcerative colitis;

KW chronic obstructive pulmonary disease; Crohn's disease.
 XX
 OS Homo sapiens.
 XX
 PN WO200058465-A2.
 XX
 PD 05-OCT-2000.
 XX
 PF 20-MAR-2000; 2000WO-US06417.
 XX
 PR 30-MAR-1999; 99US-0126839.
 XX 21-JUN-1999; 99US-0140077.
 PR 21-JUN-1999; 99US-0140136.
 PR 20-OCT-1999; 99US-0160566.
 XX 18-FEB-2000; 2000US-0183398.
 XX
 PA (ELIL) LILLY & CO ELI.
 XX
 PI Becker GW, Cohen FU, Gonzalez-deWhilt PA, Hale JE, Micranovic R;
 PI Newton CM, Nobilit TW, Rathmachalam R, Tschang SR, Wlitcher DR;
 PI Wroblewski VJ;
 XX
 DR WPI; 2000-656167/63.
 XX
 PS Disclosure; Page 113-114; 114pp; English.
 XX
 CC The present sequence represents a full length human FAS ligand inhibitory
 CC protein (FLINT). FLINT is a homologue of tumour necrosis factor receptor
 CC proteins. FLINT inhibits the binding of FAS to FAS ligand. The mature
 CC FLINT protein is modified to produce analogues, which have greater
 CC potency, longer in vivo half-lives, decreased aggregation, decreased
 CC absorption onto surfaces, increased solubility and improved ease of
 CC formulation. The FLINT analogue is useful for treating a patient
 CC suffering from disease or condition relating to abnormal apoptosis such
 CC as acute lung injury, acute respiratory distress syndrome, pulmonary
 CC fibrosis, chronic obstructive pulmonary disease, ulcerative colitis, or
 CC Crohn's disease.
 CC
 SQ Sequence 300 AA;
 Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 1 MRALEGPGLSLCLVLAIPALLPVPVAVGVAVETPTYPMDAETGRLVCAQCPPTGFVOR 60
 DB 1 MRALEGPGLSLCLVLAIPALLPVPVAVGVAVETPTYPMDAETGRLVCAQCPPTGFVOR 60
 QY 61 PCRBDSPPTGCGPPRHHTQFWNYLERCRVCNVLCGERBEERACHAHNRACRRTGFE 120
 DB 61 PCRBDSPPTGCGPPRHHTQFWNYLERCRVCNVLCGERBEERACHAHNRACRRTGFE 120
 QY 121 AHAGFCLHASCPPAGVYIAPETPSONTQCCPCPGTFSASSSSSECCOPHRNCTALGIA 180
 DB 121 AHAGFCLHASCPPAGVYIAPETPSONTQCCPCPGTFSASSSSSECCOPHRNCTALGIA 180
 QY 181 LNVPGSSSHDILCTCTGTFPLSTRVPGAEECEERAVIDFVAFODISIKRLQRLLOALEAPE 240
 DB 181 LNVPGSSSHDILCTCTGTFPLSTRVPGAEECEERAVIDFVAFODISIKRLQRLLOALEAPE 240
 QY 241 GNGPPTPRAGRAALQIKLRRLTELLGADGALLVRLLOALRVARMPGLERSVREFFLPVH 300
 DB 241 GNGPPTPRAGRAALQIKLRRLTELLGADGALLVRLLOALRVARMPGLERSVREFFLPVH 300
 RESULT 10
 AAB28559
 ID AAB28559 standard; Protein; 300 AA.

XX AAB28559;
 AC 08-FEB-2001 (first entry)
 XX
 DE Human soluble TNF receptor tnfrgt-1.
 XX
 KW Human: tumour necrosis factor like-1; TNF1; tumour necrosis factor; TNF;
 KW immunosuppressive; antiarthritic; neuroprotective; dermatological;
 KW antiinflammatory; antidiabetic; cytostatic; osteopathic; gene therapy;
 KW colon cancer; rheumatoid arthritis; septic shock; Crohn's disease;
 KW osteoporosis; autoimmune disease; myasthenia gravis;
 KW insulin-dependent diabetes mellitus.
 XX
 OS Homo sapiens.
 XX
 PN WO200060079-A2.
 PD 12-OCT-2000.
 XX
 PF 05-APR-2000; 2000MO-US09058.
 XX
 PR 05-APR-1999; 99US-0286529.
 XX
 PA (CHIR) CHIRON CORP.
 XX
 PI Tribouley C;
 XX
 DR WPI; 2000-665004/64.
 XX
 DR N-PSDB; AAC63764.
 XX
 XX
 PT Tumor necrosis factor (TNF) and TNF receptor superfamily protein
 PT members TNF-L and TNFR-L, useful for enhancing or decreasing TNF
 PT activities such as inducing cell death and lymphoid organogenesis
 XX
 OS Claim 1; Page 72; 77pp; English.
 XX
 CC The present sequence is given in a specification relating to an isolated
 CC human protein designated tumour necrosis factor like-1 (TNFL1). It may be
 CC used to induce cell death in tumours, to induce apoptosis of activated T
 CC cells, to induce inflammation, and to rescue resting T cells from
 CC apoptosis. TNF receptors are used to regulate the function of a TNF
 CC ligand which plays a role in apoptosis, inflammation, differentiation, or
 CC proliferation. Expression of the receptors can also be useful as markers
 CC for cancer, especially for colon cancer. Diseases which can be treated
 CC using ligands and/or receptors of the TNF/TNFR superfamily include
 CC rheumatoid arthritis, cancer, septic shock, Crohn's disease and
 CC osteoporosis. The polynucleotides can be used in gene delivery vehicles,
 CC for the purpose of delivering a mRNA or oligonucleotide, full-length
 CC protein, fusion protein, polypeptide, or ribozyme, or single-chain
 CC antibody, into a cell. The newly identified receptor proteins play
 CC regulatory roles in cell proliferation and/or differentiation. The
 CC receptors can also play a role in the negative regulation of
 CC osteoclastogenesis. Soluble TNFR-like receptors can be useful in the
 CC neutralisation of TNF or TNF-like ligands. A TNF-L protein can also be
 CC used to treat autoimmune diseases (myasthenia gravis and
 CC insulin-dependent diabetes mellitus), tumours, and proliferative
 CC disorders. A TNF-L or TNFR-L subgenomic polynucleotide can also be
 CC delivered to subjects for the purpose of screening test compounds for
 CC those which are useful for enhancing transfer of TNF-L subgenomic
 CC polynucleotides to the cell or for enhancing subsequent biological
 CC effects of TNF-L or TNFR-L subgenomic polynucleotides within the cell.
 XX
 SO Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 MRALEBPGSLICLVIALPALLPVPAVRGVAETPRYPMDAETGELVCAQCPRTFYOR 60
 DB 1 MRALEBPGSLICLVIALPALLPVPAVRGVAETPRYPMDAETGELVCAQCPRTFYOR 60

OY 61 PCRDSPTTCGCPPRHHYTOFMNVLERCRCYCNVLGCEEEBAAACHATNRACRCRTGPF 120
 DB 61 PCRDSPTTCGCPPRHHYTOFMNVLERCRCYCNVLGCEEEBAAACHATNRACRCRTGPF 120
 OY 121 AAAGFLEHASCPGAGVIAPEGTPSONTOCCPCPPEFSASSSSSQCCPHNRCTALGLA 180
 DB 121 AAAGFLEHASCPGAGVIAPEGTPSONTOCCPCPPEFSASSSSSQCCPHNRCTALGLA 180
 OY 181 LNVPGSSHDITCTGTFEPILSTRVPGAECECAVDFVAFODISTIKRLQRLQALEAPE 240
 DB 181 LNVPGSSHDITCTGTFEPILSTRVPGAECECAVDFVAFODISTIKRLQRLQALEAPE 240
 OY 241 GWCPTPRAGRALQLKLRRLTEILGAODGALLVRLQALRYA RMPGLERSVREPLPVH 300
 DB 241 GWCPTPRAGRALQLKLRRLTEILGAODGALLVRLQALRYA RMPGLERSVREPLPVH 300
 RESULT 11
 AAB24057
 ID AAB24057 standard; Protein; 300 AA.
 XX
 AC AAB24057;
 XX
 DT 29-JAN-2001 (first entry)
 XX
 DE Human PRO212 protein sequence SEQ ID NO:2.
 XX
 KW Human; tumour; diagnosis; neoplastic disease; neoplastic cell growth;
 KW proliferation; tumorigenesis; identification; cancer; cytostatic;
 KW neurotropic; neuroprotective; antiinflammatory; immunosuppressive;
 KW immunostimulant; antiangiogenic; leukemia; lymphoid malignancy;
 KW neuronal disorder; glial disorder; astrocytal disorder; angiogenic;
 KW hypothalamic disorder; glandular disorder; macropagal disorder;
 KW epithelial disorder; stromal disorder; blastocoeic disorder;
 KW inflammatory disorder; immunologic disorder.
 XX
 OS Homo sapiens.
 XX
 PN WO200053755-A2.
 PD 14-SEP-2000.
 XX
 PF 06-JAN-2000; 2000MO-US00376.
 XX
 PR 08-MAR-1999; 99MO-US05028.
 PR 02-JUN-1999; 99MO-US12252.
 PR 23-JUN-1999; 99US-0141037.
 PR 07-JUL-1999; 99US-0143048.
 PR 26-JUL-1999; 99US-0145698.
 PR 30-NOV-1999; 99MO-US28313.
 PR 20-DEC-1999; 99MO-US30911.
 PR 05-JAN-2000; 2000MO-US00219.
 XX
 PA (GETH) GENENTECH INC.
 XX
 PI Ashkenazi AJ, Baker KP, Goddard A, Gurney AL, Hillan KJ, Roy MA;
 PI Matanabe CK, Wood WT;
 XX
 DR WPI; 2000-572270/53.
 DR N-PSDB; AAC58367.
 XX
 PT Thirty PRO polynucleotides encoding PRO polypeptides, useful in the
 PT treatment, diagnosis and prevention of cancer -
 XX
 PS Claim 61; Fig 2; 286pp; English.
 XX
 CC The present invention describes an isolated antibody that binds to
 CC one of the human PRO proteins designated PRO212, PRO290, PRO341, PRO535,
 CC PRO619, PRO717, PRO809, PRO830, PRO848, PRO943, PRO1005, PRO1009,
 CC PRO1025, PRO1030, PRO1097, PRO1107, PRO1111, PRO1153, PRO1182, PRO1184,
 CC PRO1187, PRO1281, PRO23, PRO39, PRO834, PRO1317, PRO1710, PRO2094,
 CC PRO2145 OR PRO2198. PRO antagonists can be used to inhibit tumour cell
 CC growth. The PRO polypeptides and nucleotides are useful in the

CC treatment, diagnosis and prevention of cancer. The antibodies and other
 CC anti-tumour compounds maybe used to treat various conditions, including
 CC those characterised by overexpression and/or activation of the amplified
 CC PRO genes. Exemplary conditions or disorders to be treated with such
 CC antibodies and other compounds include benign or malignant tumours
 CC (e.g., renal, liver, kidney, bladder, breast, gastric, ovarian,
 CC colorectal, prostate, pancreatic, lung, vulva, thyroid, hepatic
 CC carcinomas, sarcomas, glioblastomas, and various head and neck tumours),
 CC leukaemias and lymphoid malignancies, other disorders such as neuronal,
 CC glial, astrocytal, hypothalamic and other glandular, macrophagal,
 CC epithelial, stromal and blastocoeleic disorders, and inflammatory,
 CC angiogenic and immunologic disorders. AAC58242 to AAC58366 represent PCR
 CC primers and hybridisation probes used in the isolation of the human PRO
 CC sequences. AAC58367 to AAC58396 and AAB24057 to AAB24089 represent human
 CC PRO polynucleotide and protein sequences given in the exemplification of
 CC the present invention.

SO Sequence 300 AA:

Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 MAALEPGSLILCTVLAIPALPVAIVGVAETPTYPMDAETGERLVCAQCPPTGTVOR 60
 DB 1 MAALEPGSLILCTVLAIPALPVAIVGVAETPTYPMDAETGERLVCAQCPPTGTVOR 60
 OY 61 PCRDSPTTCGPPRRHYTQFMNLYERCYCNVLGGEREERACATFNRRACRCGTGF 120
 DB 61 PCRDSPTTCGPPRRHYTQFMNLYERCYCNVLGGEREERACATFNRRACRCGTGF 120
 OY 121 AAAGCFLHASCPPGAGVIAIPGFSQNTCCPCPGTFSASSSSSSBQCPHNRCTALGTA 180
 DB 121 AAAGCFLHASCPPGAGVIAIPGFSQNTCCPCPGTFSASSSSSSBQCPHNRCTALGTA 180
 OY 181 LNVPSSSSHDTCTCTGTGPTLSTRVGAECERAVYDFAFODISIKRLQRLQALEAPE 240
 DB 181 LNVPSSSSHDTCTCTGTGPTLSTRVGAECERAVYDFAFODISIKRLQRLQALEAPE 240
 OY 241 GNGPFRAGRALQELKRRRLTELLGAQDGLLVRLLOARVAMPGLERSVREPLPVH 300
 DB 241 GNGPFRAGRALQELKRRRLTELLGAQDGLLVRLLOARVAMPGLERSVREPLPVH 300

RESULT 12

AAB33416
 ID AAB33416 standard: Protein; 300 AA.

AC AAB33416;

DT 29-JAN-2001 (first entry)

DE Human PRO212 protein UNQ186 SEQ ID NO:14.

XX Human; immune related disease; diagnosis; antiinflammatory; cardiant;
 KW dermatological; antlarthritic; antirheumatic; immunosuppressive;
 KW haemostatic; antithyroid; antidiabetic; nootropic; neuroprotective;
 KW antanaemic; hepatotropic; virucide; antiprotic; antiallergic;
 KW antiasthmatic; systemic lupus erythematosus; rheumatoid arthritis;
 KW osteoarthritis; spondyloarthropathy; systemic sclerosis; sarcoidosis;
 KW idiopathic inflammatory myopathy; Sjogren's syndrome; thyroiditis;
 KW systemic vasculitis; autoimmune haemolytic anaemia; diabetes mellitus;
 KW autoimmune thrombocytopenia; immune-mediated renal disease;
 KW demyelinating disease; hepatobiliary disease; Whipple's disease;
 KW inflammatory bowel disease; gluten-sensitive enteropathy;
 KW autoimmune disease; immune-mediated skin disease; allergic disease;
 KW immunological disease; transplantation associated disease;
 KW graft rejection; graft-versus-host-disease.

OS Homo sapiens.

XX WO200053758-A2.

XX

PD 14-SEP-2000.
 XX
 PF 02-MAR-2000; 2000MO-US05841.
 XX
 PR 08-MAR-1999; 99WO-US05028.
 PR 10-MAR-1999; 99US-0123618.
 PR 12-MAR-1999; 99US-0123957.
 PR 23-MAR-1999; 99US-0125775.
 PR 12-APR-1999; 99US-0128849.
 PR 20-APR-1999; 99WO-US08615.
 PR 28-APR-1999; 99US-0131445.
 PR 04-MAY-1999; 99US-0133771.
 PR 14-MAY-1999; 99US-0134287.
 PR 23-JUN-1999; 99WO-US12252.
 PR 02-JUN-1999; 99WO-US14037.
 PR 20-JUL-1999; 99US-0144758.
 PR 26-JUL-1999; 99US-0145698.
 PR 28-JUL-1999; 99US-0146222.
 PR 01-SEP-1999; 99WO-US20111.
 PR 08-SEP-1999; 99WO-US20594.
 PR 13-SEP-1999; 99WO-US20944.
 PR 15-SEP-1999; 99WO-US21090.
 PR 15-SEP-1999; 99WO-US21547.
 PR 05-OCT-1999; 99WO-US22089.
 PR 29-OCT-1999; 99US-0162506.
 PR 29-NOV-1999; 99WO-US28214.
 PR 30-NOV-1999; 99WO-US28313.
 PR 30-NOV-1999; 99WO-US28409.
 PR 01-DEC-1999; 99WO-US28301.
 PR 01-DEC-1999; 99WO-US28634.
 PR 02-DEC-1999; 99WO-US28551.
 PR 02-DEC-1999; 99WO-US28564.
 PR 16-DEC-1999; 99WO-US28665.
 PR 20-DEC-1999; 99WO-US30095.
 PR 30-DEC-1999; 99WO-US31274.
 PR 05-JAN-2000; 2000MO-US00219.
 PR 06-JAN-2000; 2000MO-US00277.
 PR 06-JAN-2000; 2000MO-US00376.
 PR 11-FEB-2000; 2000MO-US03565.
 PR 18-FEB-2000; 2000MO-US04341.
 PR 18-FEB-2000; 2000MO-US04342.
 PR 22-FEB-2000; 2000MO-US04414.
 XX
 XX (GETH) GENENTECH INC.
 PA Ashkenazi AJ, Baker KP, Goddard A, Gurney AL, Hebert C, Henzel W,
 PI Kabakoff RC, Lu Y, Pan J, Pennica D, Shelton DL, Smith V,
 PI Stewart TA, Tumas D, Watanabe CK, Wood WT, Yan M,
 DR WPI: 2000-572271/53.
 DR N-PSDB: AAC58581.
 XX
 PT Sixty four PRO polypeptides, useful in the diagnosis and treatment of
 PT immune related disorders, e.g. systemic lupus erythematosus, rheumatoid
 PT arthritis, osteoarthritis, thyroiditis and diabetes mellitus -
 XX
 Claim 33; Fig 6; 309pp; English.
 CC The present invention describes sixty four human PRO proteins which can
 CC be used in the treatment of immune related diseases. The human PRO
 CC proteins, anti-PRO antibodies, agonists and antagonists are useful for
 CC treating and diagnosing immune related disorders. The disorders are
 CC selected from systemic lupus erythematosus, rheumatoid arthritis,
 CC osteoarthritis, juvenile chronic arthritis, spondyloarthropathies,
 CC systemic sclerosis, idiopathic inflammatory myopathies, Sjogren's
 CC syndrome, systemic vasculitis, sarcoidosis, autoimmune haemolytic
 CC anaemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus,
 CC immune-mediated renal disease, demyelinating diseases of the central
 CC and peripheral nervous systems, hepatobiliary diseases, inflammatory
 CC bowel disease, gluten-sensitive enteropathy and Whipple's disease,
 CC autoimmune or immune-mediated skin diseases, allergic diseases,
 CC immunological diseases of the lung, and transplantation associated

CC diseases including graft rejection and graft-versus-host-disease.
 CC AAC58397 to AAC58578 represent PCR primers and hybridisation probes used
 CC in the isolation of human PRO sequences. AAC58579 to AAC58642 and
 CC AAB33414 to AAB33477 represent human PRO polynucleotide and protein
 CC sequences given in the exemplification of the present invention.

XX Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1,4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALGPGSLTCLVIALPALPVPVAVGVAETPTYPMDAETGERLYCAQCPGTFVQR 60
 DB 1 MRALGPGSLTCLVIALPALPVPVAVGVAETPTYPMDAETGERLYCAQCPGTFVQR 60
 QY 61 PCRDSPTTCGCPPPHHYQFMWYLERCRYCNVLCGEREEARACHATHNRACRCRTGFF 120
 DB 61 PCRDSPTTCGCPPPHHYQFMWYLERCRYCNVLCGEREEARACHATHNRACRCRTGFF 120
 QY 121 AHAGFCLERHSCPPGAGVIAAGPSPONTQCPGPGTFSASSSSSECCOPHRNCTALGIA 180
 DB 121 AHAGFCLERHSCPPGAGVIAAGPSPONTQCPGPGTFSASSSSSECCOPHRNCTALGIA 180
 QY 181 LNVPGSSSHDTLCTSGTFPLSTRVPGAECECERAVIDFVAFODISIKRLQRLQALEAPE 240
 DB 181 LNVPGSSSHDTLCTSGTFPLSTRVPGAECECERAVIDFVAFODISIKRLQRLQALEAPE 240
 QY 241 GWCPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALVARMPGLERSVERELPVH 300
 DB 241 GWCPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALVARMPGLERSVERELPVH 300

RESULT 13

AAB03621 standard; Protein; 300 AA.

XX AAB03621;

DT 03-JUN-2001 (first entry)

XX Human Fas ligand inhibitor FLINT.
 DE Human Fas ligand inhibitor; FLINT; apoptosis; autoimmune disease;
 KW Human; Fas ligand inhibitor; FLINT; apoptosis; autoimmune disease;
 KW Inflammation; infectious disease; ischemia; Alzheimer's disease;
 KW Parkinson's disease; Crohn's disease; transplantation.
 XX Homo sapiens.

XX Key Location/Qualifiers
 FH Peptide 1..29
 FT /label= signal_peptide
 FT Protein 30..300
 FT /label= mature_FLINT
 FT Domain 1..42
 FT /label= domain_1
 FT Domain 43..85
 FT /label= domain_2
 FT Domain 86..122
 FT /label= domain_3
 FT Domain 123..165
 FT /label= domain_4

XX MO200034782-A1.

XX 15-JUN-2000.

XX 07-DEC-1999; 99MO-US28696.

XX 09-DEC-1998; 98US-0111575.
 PR 09-DEC-1998; 98US-0111580.
 PR 07-JAN-1999; 99US-0115069.

PA (ELIL) LILLY & CO ELI.

XX Rostock PRJ, Song HY, Su EW;

XX WPI; 2000-431379/37.

DR N-PSDB; AAA53208.

PT Novel monkey Fas ligand inhibitor polypeptides, useful for treating
 PT inflammatory or autoimmune disease such as rheumatoid arthritis,
 PT infectious diseases such as chronic hepatitis, and
 PT Ischemia/Re-perfusion conditions -
 XX Claim 19; Page 91-93; 101pp; English.

XX The present sequence is the protein sequence of the human Fas ligand
 CC inhibitor (FLINT). The FLINT protein is involved in cell-specific
 CC apoptosis, and can be used to treat inflammatory and autoimmune diseases
 CC such as rheumatoid arthritis, inflammatory bowel disease,
 CC graft-versus-host disease, diabetes, psoriasis and Graves' disease,
 CC infectious diseases such as HIV-induced lymphopenia, fulminant viral
 CC hepatitis B/C, chronic hepatitis and cirrhosis, and H. pylori-associated
 CC ulceration, ischemia and reperfusion conditions including acute
 CC myocardial infarction, acute coronary syndrome, congestive heart failure
 CC and atherosclerosis, and Alzheimer's and Parkinson's diseases, acute lung
 CC injury and acute respiratory distress syndrome, Crohn's disease, brain
 CC trauma and injury, chronic glomerulonephritis, osteoporosis, aplastic
 CC anaemia, myelodysplasia, ulcerative colitis, Down's syndrome, and
 CC multiple sclerosis. In addition, the protein and its gene can be used to
 CC prevent apoptosis following organ transplantation.

XX Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1,4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALGPGSLTCLVIALPALPVPVAVGVAETPTYPMDAETGERLYCAQCPGTFVQR 60
 DB 1 MRALGPGSLTCLVIALPALPVPVAVGVAETPTYPMDAETGERLYCAQCPGTFVQR 60
 QY 61 PCRDSPTTCGCPPPHHYQFMWYLERCRYCNVLCGEREEARACHATHNRACRCRTGFF 120
 DB 61 PCRDSPTTCGCPPPHHYQFMWYLERCRYCNVLCGEREEARACHATHNRACRCRTGFF 120
 QY 121 AHAGFCLERHSCPPGAGVIAAGPSPONTQCPGPGTFSASSSSSECCOPHRNCTALGIA 180
 DB 121 AHAGFCLERHSCPPGAGVIAAGPSPONTQCPGPGTFSASSSSSECCOPHRNCTALGIA 180
 QY 181 LNVPGSSSHDTLCTSGTFPLSTRVPGAECECERAVIDFVAFODISIKRLQRLQALEAPE 240
 DB 181 LNVPGSSSHDTLCTSGTFPLSTRVPGAECECERAVIDFVAFODISIKRLQRLQALEAPE 240
 QY 241 GWCPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALVARMPGLERSVERELPVH 300
 DB 241 GWCPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALVARMPGLERSVERELPVH 300

RESULT 14

AAY97246 standard; Protein; 300 AA.

XX AAY97246;

DT 19-DEC-2000 (first entry)

XX M68 TNF receptor related protein.

XX M68; tumour necrosis factor; TNF; programmed cell death; apoptosis;
 KW receptor; immune response; cell differentiation; ligand; cancer;
 KW bone disease; systemic lupus erythematosus; Hashimoto's thyroiditis;
 KW Grave's disease; idiopathic myxedema; autoimmune diabetes;
 KW thrombotic thrombocytopenic purpura; multiple sclerosis;
 KW liver diseases; autoimmune gastritis; ulcerative colitis;

KM glomerulonephritis; pulmonary fibrosis; heart failure;
 KM atherosclerosis; aplastic anaemia; myelodysplastic syndromes;
 KM osteoporosis; Alzheimer's disease; Parkinson's disease; stroke;
 KM myocardial infarction; human.
 OS Homo sapiens.
 XX WO200046247-A1.
 XX 10-AUG-2000.
 XX 04-FEB-2000; 2000WO-US03037.
 XX 05-FEB-1999; 99US-0118902.
 XX 20-DEC-1999; 99US-0172754.
 XX (MERI) MERCK & CO INC.
 XX Bai C;
 XX WPI: 2000-506066/45.
 DR N-PSDB: AAA53800, AAA53801, AAA53802.
 XX Isolated human M68 nucleic acids and proteins which are part of the
 PT tumor necrosis factor receptor (TNFR) family, useful for identifying
 PT osteoporosis, Alzheimer's disease
 PS Claim 1; Page 75-76; 80pp; English.
 CC The M68 protein is a member of a family of proteins which have
 CC roles in immune responses, cell death, cell proliferation and
 CC stimulation of cell differentiation. M68 lacks a transmembrane domain
 CC and is a secreted factor suggesting that it functions as a natural
 CC inhibitor for its ligand. The altered expression pattern of M68 in a
 CC multitude of tissues suggests that M68 may play a role in cancer by
 CC binding to its ligand and blocking apoptotic cell death induced by
 CC such a ligand. This anti-apoptotic role of M68 suggests that
 CC modulators of M68 will be useful in treatment of apoptosis-related
 CC diseases such as various forms of cancer and various bone disorders.
 CC M68 nucleic acids and proteins are therefore useful for treating
 CC conditions involving atypical apoptosis and for identifying
 CC modulators of M68. Modulators of M68 are useful for treatment of
 CC cancer and other diseases associated with abnormal levels of
 CC apoptosis including systemic lupus erythematosus, Hashimoto's
 CC thyroiditis, Grave's disease, idiopathic myxedema, autoimmune
 CC diabetes, thrombotic thrombocytopenic purpura, multiple sclerosis,
 CC liver diseases, autoimmune gastritis, ulcerative colitis,
 CC glomerulonephritis, pulmonary fibrosis, heart failure,
 CC atherosclerosis, aplastic anaemia, myelodysplastic syndromes,
 CC osteoporosis, Alzheimer's disease, Parkinson's disease, stroke, and
 CC myocardial infarction.
 XX
 SQ Sequence 300 AA:
 Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1,4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 1 MRALEGGPGLSLCTLVLPALPVPVAVGVAETPTTPYPRDATTGRLVCAQCPPTFVQR 60
 DB 1 MRALEGGPGLSLCTLVLPALPVPVAVGVAETPTTPYPRDATTGRLVCAQCPPTFVQR 60
 QY 61 PCRRDSPPTGCGPPRRHYTQFWNYLERCRVCNVLCGEREEARACHATHNRACRGTGFF 120
 DB 61 PCRRDSPPTGCGPPRRHYTQFWNYLERCRVCNVLCGEREEARACHATHNRACRGTGFF 120
 QY 121 AHAGFCLHASCPCGAGVIAPCTPSQNTQCQCPPTGTSASSSSSEQCPHNRCTALGTA 180
 DB 121 AHAGFCLHASCPCGAGVIAPCTPSQNTQCQCPPTGTSASSSSSEQCPHNRCTALGTA 180
 QY 121 AHAGFCLHASCPCGAGVIAPCTPSQNTQCQCPPTGTSASSSSSEQCPHNRCTALGTA 180
 DB 121 AHAGFCLHASCPCGAGVIAPCTPSQNTQCQCPPTGTSASSSSSEQCPHNRCTALGTA 180
 QY 181 LNVPSSSHDTLCTCTGCTGPPSTRVPGAEECERAVIDVAFODISIKRLQLQLAEPE 240
 DB 181 LNVPSSSHDTLCTCTGCTGPPSTRVPGAEECERAVIDVAFODISIKRLQLQLAEPE 240

DB 181 LNVPSSSHDTLCTCTGCTGPPSTRVPGAEECERAVIDVAFODISIKRLQLQLAEPE 240
 QY 241 GGGPTPRAGRALQTLKRRRLTELLGADGALLVRLQALRVARPMPGLERSVREFFLVH 300
 DB 241 GGGPTPRAGRALQTLKRRRLTELLGADGALLVRLQALRVARPMPGLERSVREFFLVH 300
 RESULT 15
 AAY90357
 ID AAY90357 standard; Protein; 300 AA.
 XX AAY90357;
 AC AAY90357;
 DT 04-DEC-2000 (first entry)
 DE Human tumour necrosis factor receptor-6 alpha protein sequence.
 XX Human; Tumour necrosis factor receptor 6; TNFR-6alpha; TNFR-6beta;
 KW ocular neovascularisation; solid tumour; malignancy; prostate cancer;
 KW breast cancer; colon cancer; diabetic retinopathy; microbial infection;
 KW pre-maturity macular degeneration; allergy; inflammation; tissue damage;
 KW thyroid associated ophthalmopathy; cell damage; parasitic infection;
 KW bone disease; osteoporosis; atherosclerosis; cardiovascular disease;
 KW neurodegenerative disorder; Alzheimer's disease; immune disorder;
 KW graft rejection; rheumatism; liver disease; autoimmune diabetes; asthma;
 KW psoriasis; septic shock; ulcerative colitis; therapy.
 XX
 OS Homo sapiens.
 XX WO200052028-A1.
 PN 08-SEP-2000.
 PD 03-MAR-2000; 2000WO-US05686.
 PF 04-MAR-1999; 99US-0121774.
 PR 12-MAR-1999; 99US-0124092.
 PR 27-APR-1999; 99US-0131279.
 PR 30-APR-1999; 99US-0131964.
 PR 02-AUG-1999; 99US-0146371.
 PR 01-DEC-1999; 99US-0168235.
 XX
 PA (HUMA-) HUMAN GENOME SCI INC.
 XX Gentz RL, Ni J, Ebner R, Yu G, Ruben SM, Feng P;
 PI WPI: 2000-572174/53.
 DR N-PSDB: AAA37772.
 XX Nucleic acids encoding human tumour necrosis factor receptor (TNFR)
 PT proteins TNFR-6alpha and TNFR-6beta, useful for treating e.g.
 PT Alzheimer's disease, osteoporosis and graft rejection -
 XX
 PS Claim 20; Fig 1; 332pp; English.
 XX This sequence represents the human tumour necrosis factor receptor 6
 CC alpha (TNFR-6alpha) of the invention. The TNFR-6alpha and TNFR-6beta DNA
 CC and protein sequences can be used in the prevention, treatment and
 CC diagnosis of diseases associated with inappropriate TNFR expression. The
 CC nucleic acids, polypeptides, antibodies, agonists and antagonists against
 CC them may be used for the treatment of a range of conditions such as
 CC disorders associated with neovascularisation (especially ocular
 CC neovascularisation) (such as solid tumours and malignancies (e.g.
 CC prostate cancer, breast cancer and colon cancer), diabetic retinopathy
 CC and pre-maturity macular degeneration), allergies, inflammation,
 CC thyroid associated ophthalmopathy tissue/cell damage, wounds, microbial
 CC and parasitic infections, bone disease (e.g. osteoporosis),
 CC atherosclerosis, pain, cardiovascular disease (e.g. stroke),
 CC neurodegenerative disorders (e.g. Alzheimer's disease), immune
 CC disorders (e.g. graft rejection), rheumatism, liver disease,
 CC autoimmune diabetes, asthma, psoriasis, septic shock and ulcerative
 CC colitis.
 XX

50 Sequence 300 AA;

| | | | | |
|-----------------------|---------|-------------|---------|-------------|
| Query match | 100.0%; | Score 1634; | DB 21; | Length 300; |
| Best local similarity | 100.0%; | Pred No 1 | 4e-121. | |

Best Local Similarity 100.0%; Pred. No. 1.4e-121;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0

Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

| | | | |
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| Db | 1 | MRLEBPGSLICLVLPALLPVAVGVAEPTPYPMROAETGEIRLVCAQCPGTFVOR | 60 |
| QY | 61 | PCRSDPTTGCPPHRYTQFWNTYLCRCYCNVLGEEBEEBACAHATHNACRCRTGFF | 120 |
| Db | 61 | PCRSDPTTGCPPHRYTQFWNTYLCRCYCNVLGEEBEEBACAHATHNACRCRTGFF | 120 |
| QY | 121 | AHAGFCLIEASCPPGAVIAPGTPSQNTQCCPCPGTFSASSSSBEOCPHRRNTALGLA | 180 |
| Db | 121 | AHAGFCLIEASCPPGAVIAPGTPSQNTQCCPCPGTFSASSSSBEOCPHRRNTALGLA | 180 |
| QY | 181 | LNVPGSSSHDITLCISCTGFPLSTRVPGAEECERAVTFVAFODISIKRLRLQALAEPE | 240 |
| Db | 181 | LNVPGSSSHDITLCISCTGFPLSTRVPGAEECERAVTFVAFODISIKRLRLQALAEPE | 240 |
| QY | 241 | GMGPTRRAARALQIKLRRLRELLIGADGALLVRLQALVAAEMPGLETSVREBELPVH | 3000 |
| Db | 241 | GMGPTRRAARALQIKLRRLRELLIGADGALLVRLQALVAAEMPGLETSVREBELPVH | 3000 |

Search completed: July 16, 2003, 19:36:59
Job time : 40 secs

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: July 17, 2003, 15:22:24 ; Search time 38 seconds

(without alignments)
1051.979 Million cell updates/sec

Title: US-09-935-727-2

Perfect score: 1634

Sequence: 1 MRALEGPGLSLCLVLAIPA.....RVARNPGLERSVERFLPVH 300

Scoring table:

BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 73

Minimum DB seq length: 0

Maximum DB seq length: 200000000

Post-processing: Minimum Match 50%

Maximum Match 100%

Database :

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- 18: /SIDS2/gcgdata/geneSeq/geneSeq-emb1/AA1997.DAT:*
- 19: /SIDS2/gcgdata/geneSeq/geneSeq-emb1/AA1998.DAT:*
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- 21: /SIDS2/gcgdata/geneSeq/geneSeq-emb1/AA2000.DAT:*
- 22: /SIDS2/gcgdata/geneSeq/geneSeq-emb1/AA2001.DAT:*
- 23: /SIDS2/gcgdata/geneSeq/geneSeq-emb1/AA2002.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | Query Match | Length | DB ID | Description |
|------------|-------|-------------|--------|-------|-------------|
| 1 | 1634 | 100.0 | 300 | 19 | AAW66102 |
| 2 | 1634 | 100.0 | 300 | 19 | AAW63622 |
| 3 | 1634 | 100.0 | 300 | 20 | AAW03099 |
| 4 | 1634 | 100.0 | 300 | 20 | AAW42182 |
| 5 | 1634 | 100.0 | 300 | 20 | AAW17479 |
| 6 | 1634 | 100.0 | 300 | 20 | AAW06817 |
| 7 | 1634 | 100.0 | 300 | 20 | AAW97749 |
| 8 | 1634 | 100.0 | 300 | 20 | AAW95082 |
| 9 | 1634 | 100.0 | 300 | 21 | AAW19335 |
| 10 | 1634 | 100.0 | 300 | 21 | AAW28559 |

ALIGNMENTS

| | | | | | | |
|----|------|-------|-----|----|----------|---------------------|
| 11 | 1634 | 100.0 | 300 | 21 | AAW24057 | Human PRO212 prote |
| 12 | 1634 | 100.0 | 300 | 21 | AAW33416 | Human PRO212 prote |
| 13 | 1634 | 100.0 | 300 | 21 | AAW03621 | Human Fas ligand i |
| 14 | 1634 | 100.0 | 300 | 21 | AAW97246 | M68 TNF receptor r |
| 15 | 1634 | 100.0 | 300 | 21 | AAW90357 | Human tumour necro |
| 16 | 1634 | 100.0 | 300 | 21 | AAW24395 | Human PRO212 prote |
| 17 | 1634 | 100.0 | 300 | 21 | AAW96596 | Human FLINT. Homo |
| 18 | 1634 | 100.0 | 300 | 22 | AAE03568 | Human native fas l |
| 19 | 1634 | 100.0 | 300 | 22 | AAW74466 | Human FLINT native |
| 20 | 1634 | 100.0 | 300 | 22 | AAW71754 | Human NTR3. Homo |
| 21 | 1634 | 100.0 | 300 | 22 | AAW48161 | Human PRO212 poly |
| 22 | 1634 | 100.0 | 300 | 22 | AAW50903 | Human PRO212 prote |
| 23 | 1634 | 100.0 | 300 | 23 | AAE14579 | Human native FLINT |
| 24 | 1634 | 100.0 | 300 | 23 | AAE20848 | Human tumour necro |
| 25 | 1634 | 100.0 | 341 | 22 | AAW73740 | Human colon cancer |
| 26 | 1620 | 99.1 | 300 | 21 | AAW77458 | Human TNF receptor |
| 27 | 1619 | 99.1 | 300 | 21 | AAW19710 | Human Fas ligand i |
| 28 | 1619 | 99.1 | 300 | 21 | AAW96597 | Human FLINT. Homo |
| 29 | 1619 | 99.1 | 300 | 22 | AAE03570 | Human fas ligand i |
| 30 | 1619 | 99.1 | 300 | 22 | AAW83950 | Amino acid sequenc |
| 31 | 1619 | 99.1 | 300 | 22 | AAW68045 | Amino acid sequenc |
| 32 | 1619 | 99.1 | 300 | 22 | AAW68048 | Amino acid sequenc |
| 33 | 1619 | 99.1 | 300 | 23 | AAE14580 | Human FLINT analog |
| 34 | 1610 | 98.5 | 302 | 20 | AAW42183 | Human FLINT #2 pro |
| 35 | 1532 | 93.8 | 326 | 23 | ABP41980 | Human ovarian anti |
| 36 | 1509 | 92.4 | 300 | 21 | AAW03623 | Human Fas ligand i |
| 37 | 1502 | 91.9 | 300 | 21 | AAW03622 | Monkey Fas ligand i |
| 38 | 1502 | 91.9 | 300 | 21 | AAW03624 | Human Fas ligand i |
| 39 | 1491 | 91.2 | 271 | 20 | AAW42184 | Human mFLINT #1 pr |
| 40 | 1491 | 91.2 | 271 | 21 | AAW19334 | A mature human FAS |
| 41 | 1491 | 91.2 | 271 | 21 | AAW19705 | Human Fas ligand i |
| 42 | 1491 | 91.2 | 271 | 21 | AAW97247 | M68 TNF receptor r |
| 43 | 1491 | 91.2 | 271 | 21 | AAW96598 | Human mature FLINT |
| 44 | 1491 | 91.2 | 271 | 22 | AAW03567 | Human mature fas l |
| 45 | 1491 | 91.2 | 271 | 22 | AAW68044 | Amino acid sequenc |
| 46 | 1491 | 91.2 | 271 | 22 | AAW68047 | Human FLINT mature |
| 47 | 1491 | 91.2 | 271 | 22 | AAW74465 | Human FLINT mature |
| 48 | 1491 | 91.2 | 271 | 23 | AAE14578 | Human mature fas l |
| 49 | 1487 | 91.0 | 271 | 21 | AAW19709 | Human mature FLINT |
| 50 | 1487 | 91.0 | 271 | 22 | AAE03571 | Protease-resistant |
| 51 | 1487 | 91.0 | 271 | 22 | AAW74467 | Human mature fas l |
| 52 | 1487 | 91.0 | 271 | 23 | AAE14581 | Human FLINT mature |
| 53 | 1486 | 90.9 | 271 | 22 | AAE03584 | Human protease-res |
| 54 | 1486 | 90.9 | 271 | 23 | AAE14582 | Human mature fas l |
| 55 | 1485 | 90.9 | 271 | 21 | AAW96599 | Human protease-res |
| 56 | 1485 | 90.9 | 271 | 23 | AAE14583 | Human mature FLINT |
| 57 | 1485 | 90.9 | 271 | 23 | AAE14584 | Human protease-res |
| 58 | 1485 | 90.9 | 271 | 23 | AAE14586 | Human protease-res |
| 59 | 1485 | 90.9 | 271 | 23 | AAE14590 | Human protease-res |
| 60 | 1484 | 90.8 | 271 | 23 | AAE14588 | Human protease-res |
| 61 | 1484 | 90.8 | 271 | 23 | AAE14585 | Human protease-res |
| 62 | 1483 | 90.8 | 271 | 23 | AAE14587 | Human protease-res |
| 63 | 1481 | 90.6 | 271 | 21 | AAW19708 | Human protease-res |
| 64 | 1481 | 90.6 | 271 | 23 | AAE14589 | Human protease-res |
| 65 | 1475 | 90.3 | 271 | 21 | AAW19706 | Protease-resistant |
| 66 | 1471 | 90.0 | 271 | 22 | AAW68046 | Amino acid sequenc |
| 67 | 1467 | 89.8 | 271 | 21 | AAW19707 | Protease-resistant |
| 68 | 1467 | 89.8 | 273 | 20 | AAW42185 | Human mFLINT #2 pr |
| 69 | 1362 | 83.4 | 245 | 20 | AAW28449 | A human tumour nec |
| 70 | 1177 | 72.0 | 211 | 21 | AAW28560 | Human soluble TNF |
| 71 | 1153 | 70.6 | 215 | 20 | AAW93585 | Human hAPO6 protei |
| 72 | 841 | 51.5 | 153 | 20 | AAW23222 | Human TNFR superfa |
| 73 | 841 | 51.5 | 153 | 21 | AAW28554 | Human TNFR soluble |

RESULT 1

AAW66102 standard; Protein; 300 AA.

ID AAW66102; AC AAW66102;

XX

XX 02-DEC-1998 (first entry)
 DT Amino acid sequence of tumour necrosis related receptor (TR4).
 XX
 DE
 XX
 KW Human; tumour necrosis related receptor; TR4; agonist; antagonist;
 KW inhibition; chronic; acute; inflammation; arthritis; septicemia;
 KW autoimmune disease; transplant rejection; stroke; cancer;
 KW Alzheimer's disease.
 XX
 OS Homo sapiens.
 XX
 PN EP861850-A1.
 XX
 PD 02-SEP-1998.
 XX
 PF 20-JAN-1998; 98EP-0300382.
 XX
 PR 04-FEB-1997; 97US-0794796.
 XX
 PA (SMIK) SMITHKLINE BEECHAM CORP.
 XX
 PI Emery J, Tan KB, Truneh A, Young PR;
 XX
 DR WPI; 1998-508248/44.
 DR N-PSDB; AAV07654.
 XX
 PT New DNA encoding tumour necrosis related receptor - used to treat
 PT and prevent e.g. inflammation, arthritis, septicemia, autoimmune
 PT diseases, transplant rejection, infection, stroke, ischaemia, ARDS,
 PT restenosis, AIDS, bone disorders and cancer
 XX
 PS Claim 1; Fig 1; 21pp; English.
 XX
 CC This is the amino acid sequence of the human tumour necrosis related
 CC receptor (TR4), used in the method of the invention. The TR4 protein
 CC or its agonist can be used to treat a subject in need of enhanced
 CC TR4 polypeptide activity. The antagonist is used to inhibit TR4
 CC polypeptide activity. The active agents can be used for the
 CC treatment and prevention of diseases such as chronic and acute
 CC inflammation, arthritis, septicemia, autoimmune diseases, transplant
 CC rejection, stroke, cancer, Alzheimer's disease.
 CC
 XX
 SQ Sequence 300 AA;
 Query Match 100.0%; Score 1634; DB 19; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 1 MRALGFGSLTCLIVLALPALLPVAVRGVAETPTYPWRDAETGERLVCAQCPPTGVOR 60
 DB 1 MRALGFGSLTCLIVLALPALLPVAVRGVAETPTYPWRDAETGERLVCAQCPPTGVOR 60
 QY 61 PCRRDSTPTGCPGPPRHYTFWMYLERCRVCNVLGGEREEARACHATNRACRCRTGFF 120
 DB 61 PCRRDSTPTGCPGPPRHYTFWMYLERCRVCNVLGGEREEARACHATNRACRCRTGFF 120
 QY 121 AHAGFCLHASCPCPGAGVIAPTGPTSONTOCCPPGFFSASSSSSECCOPHRNCTALGTA 180
 DB 121 AHAGFCLHASCPCPGAGVIAPTGPTSONTOCCPPGFFSASSSSSECCOPHRNCTALGTA 180
 QY 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECECERAVIDFAFODISIKRLQALLAEAPE 240
 DB 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECECERAVIDFAFODISIKRLQALLAEAPE 240
 QY 241 GMPPTPRAGRAALQTLKRLRTELGAQDALLVRLQALRVARMPGLESVBERLPIVH 300
 DB 241 GMPPTPRAGRAALQTLKRLRTELGAQDALLVRLQALRVARMPGLESVBERLPIVH 300
 RESULT 2
 AAW63622
 ID AAW63622 standard; Protein; 300 AA.

XX AAW63622;
 AC 26-OCT-1998 (first entry)
 DT Human tumour necrosis factor receptor-6 alpha protein.
 XX
 DE Human tumour necrosis factor receptor-6 alpha; TNFR-6 alpha; TNFR-6 beta;
 XX Human tumour necrosis factor receptor-6 alpha; TNFR-6 alpha; TNFR-6 beta;
 KW endothelial cells; keratinocytes; normal prostate; apoptosis;
 KW prostate tumour tissue.
 XX
 OS Homo sapiens.
 XX
 FH Key Location/Qualifiers
 FH Peptide 1..30
 FT Protein 31..300
 FT /note="TNFR-6 alpha"
 FT Region 31..282
 FT /note="Soluble extracellular domain"
 XX
 PN W09830694-A2.
 XX
 PD 16-JUL-1998.
 XX
 PF 13-JAN-1998; 98WO-US00153.
 XX
 PR 14-JAN-1997; 97US-0035496.
 XX
 PA (HUMA-) HUMAN GENOME SCI INC.
 XX
 PI Ebner R, Feng P, Gentz RL, Ni J, Ruben SM, Yu G;
 XX
 DR WPI; 1998-399142/34.
 DR N-PSDB; AAV39085.
 XX
 PT Human tumour necrosis factor receptors 6-alpha and 6-beta - used in
 PT the diagnosis of immune system-related disorder(s)
 XX
 PS Claim 20; Fig 1; 91pp; English.
 XX
 CC The present sequence represents the human tumour necrosis factor
 CC receptor-6 alpha (TNFR-6 alpha) protein. The invention also provides
 CC for the TNFR-6 beta protein (AAW63623). TNFR-6 alpha and TNFR-6 beta
 CC are members of the tumour necrosis factor receptor (TNFR) family. TNFRs
 CC are expressed in endothelial cells, keratinocytes, normal prostate and
 CC prostate tumour tissue. For a number of disorders of these cells,
 CC particularly of the immune system, substantially altered (whether
 CC increased or decreased) levels of TNFR-6 alpha and/or TNFR-6 beta gene
 CC expression can be detected, therefore the TNFR-6 alpha and TNFR-6 beta
 CC polypeptides, nucleic acids and antibodies are claimed to be useful in
 CC the diagnosis of such disorders. Mutations of the TNFR-6 alpha and
 CC TNFR-6 beta genes can also be detected. The TNFR polypeptides are
 CC also claimed to be useful for identifying ligands which may be useful
 CC in the treatment of apoptosis related disorders.
 CC
 XX
 SQ Sequence 300 AA;
 Query Match 100.0%; Score 1634; DB 19; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 1 MRALGFGSLTCLIVLALPALLPVAVRGVAETPTYPWRDAETGERLVCAQCPPTGVOR 60
 DB 1 MRALGFGSLTCLIVLALPALLPVAVRGVAETPTYPWRDAETGERLVCAQCPPTGVOR 60
 QY 61 PCRRDSTPTGCPGPPRHYTFWMYLERCRVCNVLGGEREEARACHATNRACRCRTGFF 120
 DB 61 PCRRDSTPTGCPGPPRHYTFWMYLERCRVCNVLGGEREEARACHATNRACRCRTGFF 120
 QY 121 AHAGFCLHASCPCPGAGVIAPTGPTSONTOCCPPGFFSASSSSSECCOPHRNCTALGTA 180
 DB 121 AHAGFCLHASCPCPGAGVIAPTGPTSONTOCCPPGFFSASSSSSECCOPHRNCTALGTA 180

QY 181 LNVPGSSSDTLCTSGTGFPLSTRVPGAECECERAVIDFAFODISIKRLQRLQALEAPE 240
 |||||
 Db 181 LNVPGSSSDTLCTSGTGFPLSTRVPGAECECERAVIDFAFODISIKRLQRLQALEAPE 240
 |||||
 QY 241 GWCPTPRAGRAALQQLKRRRLTELLGAODGALLVRLQALRVARMPGLERSVREPLPYH 300
 |||||
 Db 241 GWCPTPRAGRAALQQLKRRRLTELLGAODGALLVRLQALRVARMPGLERSVREPLPYH 300
 |||||

RESULT 3
 ID AAY03099 standard; Protein; 300 AA.
 XX
 AC AAY03099;
 XX
 DT 09-DEC-1999 (first entry)
 XX
 DE Human lung TNF-receptor protein.
 XX
 KW Tumour necrosis factor; TNF; TNF receptor; human; lung; gene therapy;
 KW detection; immunoassay; diagnosis; disease; immune system; tumour;
 KW osteogenic system; cardiovascular system; central nervous system; asthma;
 KW peripheral nervous systems; transplant incompatibility; antitumor;
 KW rheumatoid arthritis; antiasthmatic; antiarthritic.
 XX
 OS Homo sapiens.
 XX
 FH Key Location/Qualifiers
 FT CDS 134..1036
 FT /*tag= a
 FT /product= "TNF-receptor"

DE19809978-A1.
 PD 16-SEP-1999.
 XX
 PF 09-MAR-1998; 98DE-1009978.
 XX
 PR 09-MAR-1998; 98DE-1009978.
 XX
 PA (BAD1) BASF AG.
 XX
 PI Kroegeer B;
 XX
 DR WPI: 1999-519473/44.
 DR N-PSDB; AAZ09998.
 XX
 PT New soluble member of tumor necrosis factor receptor family, useful for
 PT identification specific modulators and for treating disease e.g. tumors
 PT
 PT
 PT
 PT
 PS Claim 1; Page 8-9; 10pp; German.
 XX
 XX This invention describes a novel tumour necrosis factor (TNF) receptor
 CC (I) isolated from human lung tissue. (I) is used: (i) to raise specific
 CC antibodies (Ab); (ii) to screen for specific (ant)agonists or ligands
 CC (A), potential therapeutic agents; and (iii) therapeutically (optionally
 CC expressed from a gene therapy vector) in conditions associated with a
 CC deficit of (I). Ab are used: (a) for qualitative or quantitative
 CC detection of (I) in standard immunoassays (for diagnosis of disease, or
 CC susceptibility, or for monitoring); and (b) as therapeutic inhibitors in
 CC cases where (I) is overexpressed. Nucleic acid (II) that encodes (I) is
 CC used: (A) for recombinant production of (I); (B) also its oligonucleotide
 CC fragments, in standard hybridization and/or amplification assays; (C) as
 CC source of antisense molecules or ribozymes; and (D) to produce transgenic
 CC animals (for studying (patho)physiology of (I)). Diseases possibly
 CC associated with under- or over-expression of (I) are those of the immune,
 CC osteogenic, cardiovascular and central or peripheral nervous systems,
 CC tumors, transplant incompatibility, asthma and rheumatoid arthritis. The
 CC products of the invention have antitumor, antiasthmatic and
 CC antiarthritic activity. This sequence represents the TNF-receptor of the
 CC invention.
 XX

SQ Sequence 300 AA:
 Query Match 100.0%; Score 1634; DB 20; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALBPGSLICLVIALPALLPVPAVRGVAETPTYPMDAETGERLVCACQCPPTGVOR 60
 |||||
 Db 1 MRALBPGSLICLVIALPALLPVPAVRGVAETPTYPMDAETGERLVCACQCPPTGVOR 60
 |||||

QY 61 PCRDSPTTCGCPGPPRHVYQFMWYLERCRYCNVLCGEREERACHATNRACRKTGPF 120
 |||||
 Db 61 PCRDSPTTCGCPGPPRHVYQFMWYLERCRYCNVLCGEREERACHATNRACRKTGPF 120
 |||||

QY 121 AHAGFCLHASCPCPGAGVIAIPGSPONTCCQCPGTFSSSSSSQCPHNRCTALGIA 180
 |||||
 Db 121 AHAGFCLHASCPCPGAGVIAIPGSPONTCCQCPGTFSSSSSSQCPHNRCTALGIA 180
 |||||

QY 181 LNVPGSSSDTLCTSGTGFPLSTRVPGAECECERAVIDFAFODISIKRLQRLQALEAPE 240
 |||||
 Db 181 LNVPGSSSDTLCTSGTGFPLSTRVPGAECECERAVIDFAFODISIKRLQRLQALEAPE 240
 |||||

QY 241 GWCPTPRAGRAALQQLKRRRLTELLGAODGALLVRLQALRVARMPGLERSVREPLPYH 300
 |||||
 Db 241 GWCPTPRAGRAALQQLKRRRLTELLGAODGALLVRLQALRVARMPGLERSVREPLPYH 300
 |||||

RESULT 4
 ID AAY42182 standard; Protein; 300 AA.
 XX
 AC AAY42182;
 XX
 DT 17-DEC-1999 (first entry)
 XX
 DE Human FLINT #1 protein sequence.
 XX
 KW Human; FLINT; mFLINT; OPG3; tumour necrosis factor receptor; FasL;
 KW apoptosis; inflammation; cancer; diabetes; acute liver failure;
 KW sepsis; hepatitis; ischaemia-associated injury; hypercoagulation;
 KW reperfusion-associated injury; aplastic anaemia; differentiation;
 KW growth; myelodysplastic syndrome; pancytopenic condition;
 KW myocardial ischaemia.
 XX
 OS Homo sapiens.
 XX
 PN WO950413-A2.
 XX
 PD 07-OCT-1999.
 XX
 PF 30-MAR-1999; 99WO-US06797.
 XX
 PR 30-MAR-1998; 98US-0079856.
 PR 20-MAY-1998; 98US-0086074.
 PR 09-SEP-1998; 98US-009643.
 PR 17-DEC-1998; 98US-0112577.
 PR 18-DEC-1998; 98US-0112703.
 PR 18-DEC-1998; 98US-0112933.
 PR 22-DEC-1998; 98US-0113407.
 XX
 PA (ELIL) LILLY & CO ELI.
 XX
 PI Bumol TF, Dou S, Glasebrook AL, Gould KE, Hale JE, Heuer JG;
 PI Hui KY, Kharitonov A, Mizrahi J, Na S, Nodlitt TW, Reidy CA;
 PI Song HY, Wang J, Wu X, Zuckerman SH;
 XX
 DR WPI: 1999-591319/50.
 DR N-PSDB; AAZ25375.
 XX
 PT Use of mature protein FLINT for treating acute liver failure, inflammation,
 PT cancer, and diabetes - by prevention of FasL-Fas mediated apoptotic
 PT and proinflammatory activity
 XX

PS Claim 30: Fig 1: 99pp: English.
XX
XX
CC The present invention describes therapeutic applications of mature FLINT
CC (mFLINT) for use in the treatment of acute liver failure. Mature FLINT
CC (mFLINT), which is a member of the tumour necrosis factor receptor
CC superfamily, is used for treating acute liver failure, inflammation of
CC the liver, abnormal hepatocyte apoptosis, sepsis, a disorder associated
CC with inflammation, hepatitis, abnormal apoptosis, an ischaemia-associated
CC injury or disorder such as hypercoagulation (including use with
CC thrombolytic or anti-thrombolytic agents), reperfusion-associated injury
CC or disorder, Type I diabetes, cancer, cell damage or damage to an
CC innocent bystander tissue that is induced by a chemotherapeutic agent or
CC therapeutic irradiation, treating haematopoietic progenitor cells that
CC have been exposed to therapeutic radiation or chemotherapy, aplastic
CC anaemia, myelodysplastic syndrome or a pancytopenic condition. mFLINT is
CC also used for promoting the growth or differentiation of a haematopoietic
CC progenitor cell or CD34+ cell and preventing damage to a cardiac myocyte
CC resulting from abnormal myocardial ischaemia. The present sequence
CC represents human FLINT.
XX
SQ Sequence 300 AA:

Query Match 100.0%; Score 1634; DB 20; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.4e-121;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGGSLSLCLVIALPALLPVPAVRGVAETPTYPWMDAETGERLVCACGCPGTFFVOR 60
DB 1 MRALEGGSLSLCLVIALPALLPVPAVRGVAETPTYPWMDAETGERLVCACGCPGTFFVOR 60
QY 61 PCRDSPTTCGCPPRHHYQFMNLYERCRVCNVLGGEREEERACHATHNRRCRRTGTF 120
DB 61 PCRDSPTTCGCPPRHHYQFMNLYERCRVCNVLGGEREEERACHATHNRRCRRTGTF 120
QY 121 AAAGFCLHASPSPGAGVIAPGTPSONTCOCPPGTFSASSSSSSBOCPHNRCTALGIA 180
DB 121 AAAGFCLHASPSPGAGVIAPGTPSONTCOCPPGTFSASSSSSSBOCPHNRCTALGIA 180
QY 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECERAVIDFAFODISIKRLQRLQLALEAPE 240
DB 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECERAVIDFAFODISIKRLQRLQLALEAPE 240
QY 241 GNGPPTPRAGRALQIKLRRLTELLGAODGALLVRLLOALRVARMPGLERSVREERFLPVH 300
DB 241 GNGPPTPRAGRALQIKLRRLTELLGAODGALLVRLLOALRVARMPGLERSVREERFLPVH 300

RESULT 5
AA17479
ID AA17479 standard; Protein; 300 AA.
XX
XX
AC AA17479;
XX
XX
DT 02-AUG-1999 (first entry)
XX
XX
DE Mammalian tumour necrosis factor receptor OPG-2.
XX
XX
KM Tumour necrosis factor receptor; TNF receptor; OPG-2; Paget's disease;
KM osteopet disorder; osteoclast activity; primary osteoporosis;
KM hyperglycaemia; osteolytic metastasis; immune response; cancer.
XX
XX
OS Mammalia.
XX
XX
PN WO9926977-A1.
XX
XX
PD 03-JUN-1999.
XX
XX
PF 24-NOV-1998; 98MO-US25065.
XX
XX
PR 17-FEB-1998; 98US-0074896.
XX
XX
PR 24-NOV-1997; 97US-0066446.
XX
XX
PA (BIOL) BIOGEN INC.

XX
XX
PI Tschopp J;
XX
XX
DR WPI: 1999-347693/29.
XX
XX
DR N-PSDB; AA176052.
XX
XX
PT New tumour necrosis factor family receptor OPG-2
XX
XX
PS Claim 1: Page 18; 22pp; English.
XX
XX
CC The present sequence represents a mammalian tumour necrosis factor
CC receptor, designated OPG-2. OPG-2, is a member of the tumour necrosis
CC factor receptor family, and can be used: (i) to raise specific
CC antibodies (Ab), (ii) to treat osteopenic disorders associated with
CC excessive osteoclast activity, e.g. primary osteoporosis, Paget's
CC disease, hyperglycaemia of malignancy, or osteolytic metastases; (iii)
CC for affinity purification of cognate ligands, and (iv) to screen for
CC ligands (antagonists or agonists). Ab, or other OPG-2 blocking agents
CC such as soluble forms of the protein, are used to prevent, or reduce
CC severity of, an immune response, and for treating cancer. They can also
CC be used in diagnostic assays. The nucleic acid sequence encoding OPG-2
CC can be used as a probe to isolate related sequences from other species.
XX
SQ Sequence 300 AA:

Query Match 100.0%; Score 1634; DB 20; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.4e-121;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGGSLSLCLVIALPALLPVPAVRGVAETPTYPWMDAETGERLVCACGCPGTFFVOR 60
DB 1 MRALEGGSLSLCLVIALPALLPVPAVRGVAETPTYPWMDAETGERLVCACGCPGTFFVOR 60
QY 61 PCRDSPTTCGCPPRHHYQFMNLYERCRVCNVLGGEREEERACHATHNRRCRRTGTF 120
DB 61 PCRDSPTTCGCPPRHHYQFMNLYERCRVCNVLGGEREEERACHATHNRRCRRTGTF 120
QY 121 AAAGFCLHASPSPGAGVIAPGTPSONTCOCPPGTFSASSSSSSBOCPHNRCTALGIA 180
DB 121 AAAGFCLHASPSPGAGVIAPGTPSONTCOCPPGTFSASSSSSSBOCPHNRCTALGIA 180
QY 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECERAVIDFAFODISIKRLQRLQLALEAPE 240
DB 181 LNVPGSSSHDTLCTSGTGFPLSTRVPGAECERAVIDFAFODISIKRLQRLQLALEAPE 240
QY 241 GNGPPTPRAGRALQIKLRRLTELLGAODGALLVRLLOALRVARMPGLERSVREERFLPVH 300
DB 241 GNGPPTPRAGRALQIKLRRLTELLGAODGALLVRLLOALRVARMPGLERSVREERFLPVH 300

RESULT 6
AA106817
ID AA106817 standard; Protein; 300 AA.
XX
XX
AC AA106817;
XX
XX
DT 24-JUN-1999 (first entry)
XX
XX
DE Human DCR3 polypeptide.
XX
XX
KM DCR3 polypeptide; tumour necrosis factor receptor; TNFR; Fas ligand;
KM apoptosis; T cell mediated immune response; allergy; asthma; cancer;
KM rheumatoid arthritis; Crohn's disease; guest vs. host disease; human;
KM gene therapy.
XX
XX
OS Homo sapiens.
XX
XX
PN WO9914330-A1.
XX
XX
PD 25-MAR-1999.
XX
XX
PF 18-SEP-1998; 98MO-US19661.
XX
XX

PR 30-JUL-1998; 98US-0094640.
 PR 18-SEP-1997; 97US-0059288.
 XX
 PA (GENETH) GENENTECH INC.
 XX
 PI Ashkenazi AJ, Botstein D, Dodge KH, Goddard A, Gurney AL;
 PI Kim KU, Lawrence DA, Piltti R, Roy MA, Tumas DB;
 PI Wood WI;
 XX
 DR WPI: 1999-244032/20.
 DR N-PSDB: AAX32744.
 XX
 PT DCR3 polypeptide related to tumor necrosis factor receptor
 PS
 XX Claim 5; Fig 1; 88pp; English.
 CC This represents a human DCR3 polypeptide, a homologue of tumour necrosis
 CC factor receptor (TNFR) polypeptide. Host cells containing a vector
 CC comprising the DCR3 nucleic acid can be used for the recombinant
 CC expression of the protein. DCR3 binds to Fas ligand, so it (or its
 CC chimeras) are useful for modulating apoptosis in mammalian cells, also
 CC other Fas-ligand induced activities, particularly to inhibit T cell
 CC mediated immune responses, e.g. in treatment of allergy, asthma,
 CC rheumatoid arthritis, Crohn's disease, guest vs. host disease etc. DCR3
 CC may also be used to identify specific binding proteins, potential
 CC inhibitors. Antibodies against DCR3 are used to treat cancer,
 CC specifically of the lung and colon, also in diagnosis and for affinity
 CC purification of the protein. Detecting mutations in the gene for DCR3 is
 CC also used to diagnose cancer, or predisposition to it. DCR3 nucleic acid
 CC is useful as hybridization probe to detect genomic or related sequences;
 CC for chromosome and gene mapping; as source of antisense sequences; for
 CC expression of recombinant DCR3 and to generate transgenic animals (for
 CC development and screening of therapeutic agents), also for in vivo or
 CC ex vivo gene therapy.
 CC
 XX
 SQ Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 20; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 MRALEGGSLCLVIALPALLPVAVGVAEPTPTVWMDAETGERLVCAQCPGTEVOR 60
 DB 1 MRALEGGSLCLVIALPALLPVAVGVAEPTPTVWMDAETGERLVCAQCPGTEVOR 60
 OY 61 PCRRDSTTGGPCPPRRHYTQFWNMLERCRCNVLCGEREEBARACHATHNACRCRGFF 120
 DB 61 PCRRDSTTGGPCPPRRHYTQFWNMLERCRCNVLCGEREEBARACHATHNACRCRGFF 120
 OY 121 AHAGFCLERHASCPPGAGVIAFGTPTSQNTQCPGPGTFSASSSSSECCOPHRNCTALG 180
 DB 121 AHAGFCLERHASCPPGAGVIAFGTPTSQNTQCPGPGTFSASSSSSECCOPHRNCTALG 180
 OY 181 LNPVGSSSHDTLCTCTGCTGFPPLSTRVPAECCERAVIDFVAQDISIRRLQALBAPE 240
 DB 181 LNPVGSSSHDTLCTCTGCTGFPPLSTRVPAECCERAVIDFVAQDISIRRLQALBAPE 240
 OY 241 GWCPTPRAGRAALQIKRRRLTELLGADGALLVRLQALRVAMPGLESVRRERLPVH 300
 DB 241 GWCPTPRAGRAALQIKRRRLTELLGADGALLVRLQALRVAMPGLESVRRERLPVH 300

RESULT 7
 ID AAW97749 standard; Protein: 300 AA.
 XX
 AC AAW97749;
 XX
 DT 21-MAY-1999 (first entry)
 XX
 DE Human tumour necrosis factor receptor ZTNFR-5.
 XX
 KW ZTNFR-5; tumour necrosis factor receptor; TNFR; human;

KW cell maturation; bone cell regulation.
 XX
 OS Homo sapiens.
 XX
 FH Key
 FH Peptide
 FT 1..23
 FT /note= "signal peptide"
 FT 24..300
 FT Protein
 FT /note= "mature protein"
 FT 24..194
 FT Domain
 FT /note= "extracellular domain"
 FT 49..71
 FT Region
 FT /note= "cysteine-rich pseudo-repeat 1"
 FT 72..113
 FT Region
 FT /note= "cysteine-rich pseudo-repeat 1"
 FT 114..151
 FT Region
 FT /note= "cysteine-rich pseudo-repeat 1"
 FT 152..194
 FT /note= "cysteine-rich pseudo-repeat 1"

W09904001-A1.
 PD 28-JAN-1999.
 XX
 XX 21-JUL-1998; 98WO-US15072.
 XX
 XX 21-JUL-1997; 97US-0053203.
 XX
 XX (ZYMO) ZYMOGENETICS INC.
 XX
 XX Farrah TM;
 DR WPI: 1999-132245/11.
 DR N-PSDB: AAX07226.
 XX

Novel tumour necrosis factor receptor ZTNFR5 - useful for
 regulating maturation of TNF-ligand bearing cells
 Claim 1; Page 84-85; 109pp; English.

This polypeptide comprises a new, secreted tumour necrosis factor
 receptor (see AAW97749), designated ZTNFR-5. Novel ZTNFR-5 encoding
 CC polynucleotides and polypeptides were initially identified by
 CC querying an expressed sequence tag (EST) database for sequences
 CC homologous to conserved motifs within the TNF receptor family.
 CC Based on this search, a contig of 16 ESTs (see AAX07226) was
 CC constructed. ZTNFR-5 polypeptides comprise 4 cysteine-rich repeats
 CC (see also AAW97750-55) that are homologous to other TNF receptors, in
 CC particular the soluble, secreted TNF receptor osteoprotegerin.
 CC ZTNFR-5 polypeptide can be prepared by recombinant methods. The
 CC polypeptide, especially the extracellular domain, can be used to
 CC generate a soluble variant of ZTNFR-5. The polypeptides and
 CC nucleic acids can be used to screen for ligands, agonists and
 CC antagonists of ZTNFR-5. The polypeptides can be used in bone cell
 CC regulation and to regulate the maturation of TNF ligand-bearing
 CC cells such as T- or B-cells, lymphocytes, peripheral blood
 CC mononuclear cells, polymorphonuclear leukocytes, fibroblasts or
 CC haematopoietic cells.
 CC
 XX
 SQ Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 20; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 MRALEGGSLCLVIALPALLPVAVGVAEPTPTVWMDAETGERLVCAQCPGTEVOR 60
 DB 1 MRALEGGSLCLVIALPALLPVAVGVAEPTPTVWMDAETGERLVCAQCPGTEVOR 60
 OY 61 PCRRDSTTGGPCPPRRHYTQFWNMLERCRCNVLCGEREEBARACHATHNACRCRGFF 120
 DB 61 PCRRDSTTGGPCPPRRHYTQFWNMLERCRCNVLCGEREEBARACHATHNACRCRGFF 120

QY 121 AHAGFCLIEHASCPPGAGVIAPGTPSONTCQPCPPGTFSSASSSSSECCQPHRNCALGLA 180
 DB 121 AHAGFCLIEHASCPPGAGVIAPGTPSONTCQPCPPGTFSSASSSSSECCQPHRNCALGLA 180
 QY 181 LNPVSSSHDTLCTSCGFPFLSTRVPGAECERAVIDFAFODISIKRLORLQALEAPE 240
 DB 181 LNPVSSSHDTLCTSCGFPFLSTRVPGAECERAVIDFAFODISIKRLORLQALEAPE 240
 QY 241 GNGPPTPRAGRAALQALKRRLTELLGADGALLVRLQALRVARMGELERSVERELPVH 300
 DB 241 GNGPPTPRAGRAALQALKRRLTELLGADGALLVRLQALRVARMGELERSVERELPVH 300

RESULT 8
 AAW95082 standard; Protein: 300 AA.
 ID AAW95082;
 AC AAW95082;
 XX
 XX
 DT 20-MAY-1999 (first entry)
 DE Orphan receptor (HUMAN NTR-1) polypeptide.
 DE
 XX
 KM HUMAN NTR-1, orphan receptor; osteoprotegerin; OPG; TNFR; human;
 KM tumour necrosis factor receptor; muscle disorder; bone mass; screening;
 KM muscle metabolism; binding agent; cognate ligand.
 XX
 OS Homo sapiens.
 XX
 PN WO9907738-A2.
 XX
 PD 18-FEB-1999.
 XX
 PF 04-AUG-1998; 98WO-US16202.
 XX
 PR 06-AUG-1997; 97US-0054869.
 XX
 PA (PROC) PROCTER & GAMBLE CO.
 PA (REG-) REGENERON PHARM INC.
 XX
 PI Maslowski PJ, Morris J, Valenzuela DM;
 DR WPI, 1999-167365/14.
 DR N-PSDB; AAX22300.
 XX
 PT Novel orphan human receptor polypeptide and nucleic acid - useful as
 PT diagnostic reagents and for treatment of muscle disorders
 PS Claim 7; Page 21; 23pp; English.
 XX
 CC This represents a HUMAN NTR-1 polypeptide, a novel orphan receptor. The
 CC protein is related to osteoprotegerin (OPG) and to tumour necrosis factor
 CC receptor (TNFR). Host cells transformed with a vector comprising the
 CC HUMAN NTR-1 nucleic acid are used for the recombinant expression of the
 CC protein. HUMAN NTR-1 proteins and antibodies immuno specific for the
 CC protein are useful for diagnosis and treatment of humans and animals,
 CC especially muscle disorders, as the receptor is involved in regulation of
 CC bone mass and muscle metabolism. HUMAN NTR-1 receptors are also useful
 CC for screening for novel binding agents, and cognate ligands, which may be
 CC used to treat disorders associated with HUMAN NTR-1 imbalance.
 XX
 SQ Sequence 300 AA:
 Query Match 100.0%; Score 1634; DB 20; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALBEGPGLSLCLVLALPALLPVPVAVGVAETPTYPWRDAETGERLYVCAQCPCPGTFVOR 60
 DB 1 MRALBEGPGLSLCLVLALPALLPVPVAVGVAETPTYPWRDAETGERLYVCAQCPCPGTFVOR 60
 QY 61 PCRBDPTTCGPPPHHTYQFWNYLERCRVCNVLGEBREEARACHATNRACRCRTGFF 120
 DB 61 PCRBDPTTCGPPPHHTYQFWNYLERCRVCNVLGEBREEARACHATNRACRCRTGFF 120

DB 61 PCRBDPTTCGPPPHHTYQFWNYLERCRVCNVLGEBREEARACHATNRACRCRTGFF 120
 QY 121 AHAGFCLIEHASCPPGAGVIAPGTPSONTCQPCPPGTFSSASSSSSECCQPHRNCALGLA 180
 DB 121 AHAGFCLIEHASCPPGAGVIAPGTPSONTCQPCPPGTFSSASSSSSECCQPHRNCALGLA 180
 QY 181 LNPVSSSHDTLCTSCGFPFLSTRVPGAECERAVIDFAFODISIKRLORLQALEAPE 240
 DB 181 LNPVSSSHDTLCTSCGFPFLSTRVPGAECERAVIDFAFODISIKRLORLQALEAPE 240
 QY 241 GNGPPTPRAGRAALQALKRRLTELLGADGALLVRLQALRVARMGELERSVERELPVH 300
 DB 241 GNGPPTPRAGRAALQALKRRLTELLGADGALLVRLQALRVARMGELERSVERELPVH 300

RESULT 9
 AAB19335 standard; Protein: 300 AA.
 ID AAB19335;
 AC AAB19335;
 XX
 XX
 DT 19-FEB-2001 (first entry)
 DE A full length human FAS Ligand Inhibitory Protein (FLINT).
 DE
 XX
 KM Human; FAS Ligand Inhibitory Protein; FLINT; analogue; apoptosis;
 KM tumour necrosis factor receptor; acute lung injury; pulmonary fibrosis;
 KM acute respiratory distress syndrome; ulcerative colitis;
 KM chronic obstructive pulmonary disease; Crohn's disease.
 XX
 OS Homo sapiens.
 XX
 PN WO200058465-A2.
 XX
 PD 05-OCT-2000.
 XX
 PF 20-MAR-2000; 2000WO-US06417.
 XX
 PR 30-MAR-1999; 99US-0126839.
 PR 21-JUN-1999; 99US-0140077.
 PR 20-OCT-1999; 99US-0140156.
 PR 18-FEB-2000; 2000US-0183398.
 XX
 PA (ELIT) LILLY & CO ELIT.
 XX
 PI Becker GW, Cohen EJ, Gonzalez-dewhitt PA, Hale JR, Micanovic R;
 PI Newton CM, Noblitt TW, Rathmacnam R, Tschang SR, Witcher DR;
 PI Wobrowski VJ;
 DR WPI; 2000-656167/63.
 XX
 PT FAS ligand Inhibitory protein analogs useful for treating abnormal
 PT apoptosis related diseases e.g. acute lung injury, pulmonary fibrosis,
 PT chronic obstructive pulmonary disease ulcerative colitis or Crohn's
 PT disease
 PS Disclosure; Page 113-114; 114pp; English.
 XX
 CC The present sequence represents a full length human FAS ligand inhibitory
 CC protein (FLINT). FLINT is a homologue of tumour necrosis factor receptor
 CC proteins. FLINT inhibits the binding of FAS to FAS ligand. The mature
 CC FLINT protein is modified to produce analogues, which have greater
 CC potency, longer in vivo half-lives, decreased aggregation, decreased
 CC absorption onto surfaces, increased solubility and improved ease of
 CC formulation. The FLINT analogue is useful for treating a patient
 CC suffering from disease or condition relating to abnormal apoptosis such
 CC as acute lung injury, acute respiratory distress syndrome, pulmonary
 CC fibrosis, chronic obstructive pulmonary disease, ulcerative colitis, or
 CC Crohn's disease.
 XX
 SQ Sequence 300 AA:

Query Match 100.0%; Score 1634; DB 21; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.4e-121;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGSLSLICLVIALPALPPAVAGVAFETPTYPWRDAETGERLYCACCPGTFYQR 60
DB 1 MRALEGSLSLICLVIALPALPPAVAGVAFETPTYPWRDAETGERLYCACCPGTFYQR 60
QY 61 PCRRDSPPTGCPCPRRHYTOPFWNYLERCRVCNVLCGEREEBARACHATHNRACRCRGFF 120
DB 61 PCRRDSPPTGCPCPRRHYTOPFWNYLERCRVCNVLCGEREEBARACHATHNRACRCRGFF 120
QY 121 AHAGFCLSHASCPRGAGVIAAGTPSQTQCCPCPGTFSSASSSSSECCQPHRNCATAGLA 180
DB 121 AHAGFCLSHASCPRGAGVIAAGTPSQTQCCPCPGTFSSASSSSSECCQPHRNCATAGLA 180
QY 181 LNVGSSSHDPLCTSCGFPPLSTRVPAEBCERAVIDFVAQDISIKRLQLLQALEAPE 240
DB 181 LNVGSSSHDPLCTSCGFPPLSTRVPAEBCERAVIDFVAQDISIKRLQLLQALEAPE 240
QY 241 GWGPTPRAGRAALQKLRRLTELLGAODGALLVRLQALRVAMPGLERSVRERFPLVH 300
DB 241 GWGPTPRAGRAALQKLRRLTELLGAODGALLVRLQALRVAMPGLERSVRERFPLVH 300

RESULT 10
AAB28559 standard; protein: 300 AA.

XX AAB28559;
XX 08-FEB-2001 (first entry)
XX Human soluble TNF receptor tnfr-1.
XX DE
XX KW Human: tumour necrosis factor like-1; TNF1; tumour necrosis factor; TNF;
KW immunosuppressive; antiarthritic; neuroprotective; dermatological;
KW antiinflammatory; antidiabetic; cytostatic; osteopathic; gene therapy;
KW colon cancer; rheumatoid arthritis; septic shock; Crohn's disease;
KW osteoporosis; autoimmune disease; myasthenia gravis;
KW insulin-dependent diabetes mellitus.
XX OS
XX Homo sapiens.
XX PN
XX W0200060079-A2.
XX PD
XX 12-OCY-2000.
XX PF 05-APR-2000; 2000WO-US09058.
XX PR 05-APR-1999; 99US-0286529.
XX PA (CHIR) CHIRON CORP.
XX PI
XX Triboley C;
XX DR WPI: 2000-665004/64.
XX N-PSDB; AAC63764.
XX PT Tumour necrosis factor (TNF) and TNF receptor superfamily protein
XX PT members TNF-L and TNFR-L, useful for enhancing or decreasing TNF
XX PT activities such as inducing cell death and lymphoid organogenesis
XX
XX Claim 1; Page 72; 77pp; English.
XX
XX The present sequence is given in a specification relating to an isolated
XX human protein designated tumour necrosis factor like-1 (TNF1). It may be
XX used to induce cell death in tumours, to induce apoptosis of activated T
XX cells, to induce inflammation, and to rescue resting T cells from
XX apoptosis. TNF receptors are used to regulate the function of a TNF
XX ligand which plays a role in apoptosis, inflammation, differentiation, or
XX proliferation. Expression of the receptors can also be useful as markers
XX for cancer, especially for colon cancer. Diseases which can be treated

CC using ligands and/or receptors of the TNF/TNFR superfamily include
CC rheumatoid arthritis, cancer, septic shock, Crohn's disease and
CC osteoporosis. The polynucleotides can be used in gene delivery vehicles,
CC for the purpose of delivering a mRNA or oligonucleotide, full-length
CC protein, fusion protein, polypeptide, or ribozyme, or single-chain
CC antibody, into a cell. The newly identified receptor proteins play
CC regulatory roles in cell proliferation and/or differentiation. The
CC receptors can also play a role in the negative regulation of
CC osteoclastogenesis. Soluble TNFR-like receptors can be useful in the
CC neutralisation of TNF or TNF-like ligands. A TNF-L protein can also be
CC used to treat autoimmune diseases (myasthenia gravis and
CC insulin-dependent diabetes mellitus), tumours, and proliferative
CC disorders. A TNF-L or TNFR-L subgenomic polynucleotide can also be
CC delivered to subjects for the purpose of screening test compounds for
CC those which are useful for enhancing transfer of TNF-L subgenomic
CC polynucleotides to the cell or for enhancing subsequent biological
CC effects of TNF-L or TNFR-L subgenomic polynucleotides within the cell.
XX
XX Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 21; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.4e-121;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGSLSLICLVIALPALPPAVAGVAFETPTYPWRDAETGERLYCACCPGTFYQR 60
DB 1 MRALEGSLSLICLVIALPALPPAVAGVAFETPTYPWRDAETGERLYCACCPGTFYQR 60
QY 61 PCRRDSPPTGCPCPRRHYTOPFWNYLERCRVCNVLCGEREEBARACHATHNRACRCRGFF 120
DB 61 PCRRDSPPTGCPCPRRHYTOPFWNYLERCRVCNVLCGEREEBARACHATHNRACRCRGFF 120
QY 121 AHAGFCLSHASCPRGAGVIAAGTPSQTQCCPCPGTFSSASSSSSECCQPHRNCATAGLA 180
DB 121 AHAGFCLSHASCPRGAGVIAAGTPSQTQCCPCPGTFSSASSSSSECCQPHRNCATAGLA 180
QY 181 LNVGSSSHDPLCTSCGFPPLSTRVPAEBCERAVIDFVAQDISIKRLQLLQALEAPE 240
DB 181 LNVGSSSHDPLCTSCGFPPLSTRVPAEBCERAVIDFVAQDISIKRLQLLQALEAPE 240
QY 241 GWGPTPRAGRAALQKLRRLTELLGAODGALLVRLQALRVAMPGLERSVRERFPLVH 300
DB 241 GWGPTPRAGRAALQKLRRLTELLGAODGALLVRLQALRVAMPGLERSVRERFPLVH 300

RESULT 11
AAB24057 standard; protein: 300 AA.

XX AAB24057;
XX 29-JAN-2001 (first entry)
XX Human PRO212 protein sequence SEQ ID NO:2.
XX DE
XX KW Human: tumour; diagnosis; neoplastic disease; neoplastic cell growth;
KW proliferation; tumorigenesis; identification; cancer; cytostatic;
KW neurotropic; neuroprotective; antiinflammatory; immunosuppressive;
KW immunostimulant; antileukemic; leukaemia; lymphoid malignancy;
KW neuronal disorder; gliad disorder; astrocytal disorder; angiogenic;
KW hypothalamic disorder; glandular disorder; macropagal disorder;
KW epithelial disorder; stromal disorder; blastocoeleic disorder;
KW inflammatory disorder; immunologic disorder.
XX OS
XX Homo sapiens.
XX PN
XX W0200053755-A2.
XX PD 14-SEP-2000.
XX PF 06-JAN-2000; 2000WO-US00376.
XX PR 08-MAR-1999; 99WO-US05028.

PR 02-JUN-1999; 99WO-US12252.
PR 23-JUN-1999; 99US-0141037.
PR 07-JUL-1999; 99US-0143048.
PR 26-JUL-1999; 99US-0145698.
PR 30-NOV-1999; 99WO-US28313.
PR 20-DEC-1999; 99WO-US30911.
PR 05-JAN-2000; 2000WO-US00219.
XX
XX (GETH) GENENTECH INC.
XX
XX Ashkenazi AJ, Baker KP, Goddard A, Gurney AL, Hillan KJ, Roy MA;
PI Metanabe CK, Wood WI;
XX
XX WPI; 2000-572270/53.
DR N-PSDB; AAC58367.
XX
XX Thiry PRO polynucleotides encoding PRO polypeptides, useful in the
PT treatment, diagnosis and prevention of cancer -
PS
PS Claim 61; Fig 2; 286pp; English.

CC The present invention describes an isolated antibody that binds to
CC one of the human PRO proteins designated PRO212, PRO290, PRO341, PRO355,
CC PRO619, PRO717, PRO809, PRO830, PRO848, PRO943, PRO1005, PRO1009,
CC PRO1025, PRO1030, PRO1097, PRO1107, PRO1111, PRO1153, PRO1182, PRO1184,
CC PRO1187, PRO1281, PRO23, PRO39, PRO834, PRO1317, PRO1710, PRO2094,
CC PRO2145 OR PRO2198. PRO antagonists can be used to inhibit tumour cell
CC growth. The PRO polypeptides and nucleotides are useful in the
CC treatment, diagnosis and prevention of cancer. The antibodies and other
CC anti-tumour compounds may be used to treat various conditions, including
CC those characterised by overexpression and/or activation of the amplified
CC PRO genes. Exemplary conditions or disorders to be treated with such
CC antibodies and other compounds include benign or malignant tumours
CC (e.g., renal, liver, kidney, bladder, breast, gastric, ovarian,
CC colorectal, prostate, pancreatic, lung, vulva, thyroid, hepatic
CC carcinomas, sarcomas, glioblastomas, and various head and neck tumours),
CC leukemias and lymphoid malignancies, other disorders such as neuronal,
CC glioma, astrocytic, hypothalamic and other glandular, macrophagal,
CC epithelial, stromal and blastocoele disorders, and inflammatory,
CC angiogenic and immunologic disorders. AAC58242 to AAC58366 represent PCR
CC primers and hybridisation probes used in the isolation of the human PRO
CC sequences. AAC58367 to AAC58396 and AAB24057 to AAB24089 represent human
CC PRO polynucleotide and protein sequences given in the exemplification of
CC the present invention.
XX
XX Sequence 300 AA:

Query Match 100.0%; Score 1634; DB 21; Length 300;
Best Local Similarity 100.0%; Pred. No. 1.4e-121;
Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGGSLTLCVLAIPALPVPVAVRGVAETPTYPWRAETGERLVCAQCPGTFVOR 60
DB 1 MRALEGGSLTLCVLAIPALPVPVAVRGVAETPTYPWRAETGERLVCAQCPGTFVOR 60
QY 61 PCRRDSEPTTCGPPRRHYTOFWNYLERCRYCNVLCGERREBARCAHNRACRCRTGFF 120
DB 61 PCRRDSEPTTCGPPRRHYTOFWNYLERCRYCNVLCGERREBARCAHNRACRCRTGFF 120
QY 121 AHAGFCLERHASCPPGAGVIAAGPSONTOCOPCPGTFSSSSSSSECCOPHRNCTALGLA 180
DB 121 AHAGFCLERHASCPPGAGVIAAGPSONTOCOPCPGTFSSSSSSSECCOPHRNCTALGLA 180
QY 181 LNVGSSSHDTLCTSGTGFPLSTRVGAECERAVIDVFAFODISIKRLQRLQALEAPE 240
DB 181 LNVGSSSHDTLCTSGTGFPLSTRVGAECERAVIDVFAFODISIKRLQRLQALEAPE 240
QY 241 GWCPTPRAGRAALQLLRRRLTELLCAQDQALLVRLQALVARMPGLERSVERELPVH 300
DB 241 GWCPTPRAGRAALQLLRRRLTELLCAQDQALLVRLQALVARMPGLERSVERELPVH 300

RESULT 12

AAB33416
ID AAB33416 standard; Protein: 300 AA.
XX
XX AAB33416;
AC
XX
DT 29-JAN-2001 (first entry)
XX
XX Human PRO212 protein UNQ186 SEQ ID NO:14.
DE
XX Human: immune related disease; diagnosis; antiinflammatory; cardiant;
KW hemostatic; antithyroid; antidiabetic; noctropic; neuroprotective;
KW antianemic; hepatocytic; virucide; antiporiatic; antiallergic;
KW antiaesthetic; systemic lupus erythematosus; rheumatoid arthritis;
KW osteoarthritis; spondyloarthritis; systemic sclerosis; sarcoidosis;
KW idiopathic inflammatory myopathy; Sjogren's syndrome; thyroiditis;
KW systemic vasculitis; autoimmune haemolytic anaemia; diabetes mellitus;
KW autoimmune thrombocytopenia; immune-mediated renal disease;
KW demyelinating disease; hepatobiliary disease; Whipple's disease;
KW inflammatory bowel disease; gluten-sensitive enteropathy;
KW autoimmune disease; immune-mediated skin disease; allergic disease;
KW immunological disease; transplantation associated disease;
KW graft rejection; graft-versus-host-disease.

XX Homo sapiens.
XX WO200053758-A2.
XX
XX 14-SEP-2000.

XX 02-MAR-2000; 2000WO-US05841.
XX
XX 08-MAR-1999; 99WO-US05028.
XX 10-MAR-1999; 99US-0123618.
XX 12-MAR-1999; 99US-0123957.
XX 23-MAR-1999; 99US-0125775.
XX 12-APR-1999; 99US-0128849.
XX 20-APR-1999; 99WO-US08615.
XX 28-APR-1999; 99US-0131445.
XX 04-MAY-1999; 99US-0132371.
XX 14-MAY-1999; 99US-0134287.
XX 02-JUN-1999; 99WO-US12252.
XX 23-JUN-1999; 99US-0141037.
XX 20-JUL-1999; 99US-0144758.
XX 26-JUL-1999; 99US-0145698.
XX 28-JUL-1999; 99US-0146222.
XX 01-SEP-1999; 99WO-US20111.
XX 08-SEP-1999; 99WO-US20594.
XX 13-SEP-1999; 99WO-US20944.
XX 15-SEP-1999; 99WO-US21090.
XX 15-SEP-1999; 99WO-US21547.
XX 05-OCT-1999; 99WO-US23089.
XX 29-OCT-1999; 99US-0162506.
XX 29-NOV-1999; 99WO-US28214.
XX 30-NOV-1999; 99WO-US28313.
XX 30-NOV-1999; 99WO-US28409.
XX 01-DEC-1999; 99WO-US28301.
XX 01-DEC-1999; 99WO-US28634.
XX 02-DEC-1999; 99WO-US28511.
XX 02-DEC-1999; 99WO-US28564.
XX 02-DEC-1999; 99WO-US28565.
XX 16-DEC-1999; 99WO-US30095.
XX 20-DEC-1999; 99WO-US30099.
XX 30-DEC-1999; 99WO-US31274.
XX 05-JAN-2000; 2000WO-US00219.
XX 06-JAN-2000; 2000WO-US00277.
XX 06-JAN-2000; 2000WO-US00376.
XX 11-FEB-2000; 2000WO-US03565.
XX 18-FEB-2000; 2000WO-US04341.
XX 18-FEB-2000; 2000WO-US04342.
XX 22-FEB-2000; 2000WO-US04414.

(GETH) GENENTECH INC.

XX Ashkenazi AJ, Baker KP, Goddard A, Gurney AL, Hebert C, Henzel W;
 PI Kabakoff RC, Lu Y, Pan J, Pennica D, Shelton DL, Smith V;
 PI Stewart TA, Tamas D, Matanabe CK, Wood WL, Yan M;
 DR WPI: 2000-572271/53.
 DR N-PSDB: AAC58581.

XX Sixty four PRO polypeptides, useful in the diagnosis and treatment of
 PT immune related disorders, e.g. systemic lupus erythematosus, rheumatoid
 PT arthritis, osteoarthritis, thyroiditis and diabetes mellitus -

XX Claim 33: Fig 6; 309pp; English.

XX The present invention describes sixty four human PRO proteins which can
 CC be used in the treatment of immune related diseases. The human PRO
 CC proteins, anti-PRO antibodies, agonists and antagonists are useful for
 CC treating and diagnosing immune related disorders. The disorders are
 CC selected from systemic lupus erythematosus, rheumatoid arthritis,
 CC osteoarthritis, juvenile chronic arthritis, spondyloarthropathies,
 CC systemic sclerosis, idiopathic inflammatory myopathies, Sjogren's
 CC syndrome, systemic vasculitis, sarcoidosis, autoimmune hemolytic
 CC anaemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus,
 CC immune-mediated renal disease, demyelinating diseases of the central
 CC and peripheral nervous systems, hepatobiliary diseases, inflammatory
 CC bowel disease, gluten-sensitive enteropathy and Whipple's disease,
 CC autoimmune or immune-mediated skin diseases, allergic diseases,
 CC immunological diseases of the lung, and transplantation associated
 CC diseases including graft rejection and graft-versus-host-disease.
 CC AAC58397 to AAC58578 represent PCR primers and hybridisation probes used
 CC in the isolation of human PRO sequences. AAC58579 to AAC58642 and
 CC AAB33414 to AAB33477 represent human PRO polynucleotide and protein
 CC sequences given in the exemplification of the present invention.

XX Sequence 300 AA:

Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 MRALEGPSLLCLVLLPALLPVPVAVGVAETPTYPWRDAETGERLYCAOCPPTGVQR 60
 DB 1 MRALEGPSLLCLVLLPALLPVPVAVGVAETPTYPWRDAETGERLYCAOCPPTGVQR 60
 OY 61 PCRRDSPPTGCPPRRHHTOFTWNYLERRCYCNVLCGEERERACHAHNRCRCRTGFF 120
 DB 61 PCRRDSPPTGCPPRRHHTOFTWNYLERRCYCNVLCGEERERACHAHNRCRCRTGFF 120
 OY 121 AHAGFCLHASCPCPGAGVIAGPTPSQNTQCPCPPGTFSASSSSSEOCQPHRNCATGIA 180
 DB 121 AHAGFCLHASCPCPGAGVIAGPTPSQNTQCPCPPGTFSASSSSSEOCQPHRNCATGIA 180
 OY 121 AHAGFCLHASCPCPGAGVIAGPTPSQNTQCPCPPGTFSASSSSSEOCQPHRNCATGIA 180
 DB 121 AHAGFCLHASCPCPGAGVIAGPTPSQNTQCPCPPGTFSASSSSSEOCQPHRNCATGIA 180
 OY 181 LNVGSSSHDPLTCTSGTFPLSTRVPGAECEBRAVIDFVAPODISIKRLQRLLOALEAPE 240
 DB 181 LNVGSSSHDPLTCTSGTFPLSTRVPGAECEBRAVIDFVAPODISIKRLQRLLOALEAPE 240
 OY 241 GWMGPTPRAGRAALQKLRRRLTELIGADGALLVRLQALVAPRMPGLERSVREFFLVH 300
 DB 241 GWMGPTPRAGRAALQKLRRRLTELIGADGALLVRLQALVAPRMPGLERSVREFFLVH 300

RESULT 13
 AAB03621
 ID AAB03621 standard; Protein: 300 AA.

XX AAB03621;
 DT 03-JAN-2001 (first entry)

XX Human Fas ligand inhibitor FLINT.

XX Human Fas ligand inhibitor; FLINT; apoptosis; autoimmune disease;
 KW Inflammation; infectious disease; ischaemia; Alzheimer's disease;

KW Parkinson's disease; Crohn's disease; transplantation.
 XX Homo sapiens.

XX Key Location/Qualifiers
 FH Peptide 1..29
 FT /label= signal_peptide
 FT Protein 30..300
 FT /label= mature_FLINT
 FT Domain 1..42
 FT /label= domain_1
 FT Domain 43..85
 FT /label= domain_2
 FT Domain 86..122
 FT /label= domain_3
 FT Domain 123..165
 FT /label= domain_4

PD WO200034782-A1.
 PD 15-JUN-2000.

PF 07-DEC-1999; 99WO-US28696.

PR 09-DEC-1998; 98US-0111575.
 PR 09-DEC-1998; 98US-0111580.
 PR 07-JAN-1999; 99US-0115069.

PA (ELI) LILLY & CO ELI.

DR Rosteck PRJ, Song HY, Su EW;

DR WPI: 2000-433379/37.
 DR N-PSDB: AAA53208.

XX Novel monkey Fas ligand inhibitor polypeptides, useful for treating
 PT inflammatory or autoimmune disease such as rheumatoid arthritis,
 PT infectious diseases such as chronic hepatitis, and
 PT ischaemia/Re-perfusion conditions -

XX Claim 19; Page 91-93; 101pp; English.

XX The present sequence is the protein sequence of the human Fas ligand
 CC inhibitor (FLINT). The FLINT protein is involved in cell-specific
 CC apoptosis, and can be used to treat inflammatory and autoimmune diseases
 CC such as rheumatoid arthritis, inflammatory bowel disease,
 CC graft-versus-host disease, diabetes, psoriasis and Graves' disease,
 CC infectious diseases such as HIV-induced lymphopenia, fulminant viral
 CC hepatitis B/C, chronic hepatitis and cirrhosis, and H. pylori-associated
 CC ulceration, ischaemia and reperfusion conditions including acute
 CC myocardial infarction, acute coronary syndrome, congestive heart failure
 CC and atherosclerosis, and Alzheimer's and Parkinson's diseases, acute lung
 CC injury and acute respiratory distress syndrome, Crohn's disease, brain
 CC trauma and injury, chronic glomerulonephritis, osteoporosis, aplastic
 CC anaemia, myelodysplasia, ulcerative colitis, Down's syndrome, and
 CC multiple sclerosis. In addition, the protein and its gene can be used to
 CC prevent apoptosis following organ transplantation.

XX Sequence 300 AA:

Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 MRALEGPSLLCLVLLPALLPVPVAVGVAETPTYPWRDAETGERLYCAOCPPTGVQR 60
 DB 1 MRALEGPSLLCLVLLPALLPVPVAVGVAETPTYPWRDAETGERLYCAOCPPTGVQR 60

OY 61 PCRRDSPPTGCPPRRHHTOFTWNYLERRCYCNVLCGEERERACHAHNRCRCRTGFF 120
 DB 61 PCRRDSPPTGCPPRRHHTOFTWNYLERRCYCNVLCGEERERACHAHNRCRCRTGFF 120

OY 121 AHAGFCLHASCPCPGAGVIAGPTPSQNTQCPCPPGTFSASSSSSEOCQPHRNCATGIA 180
 DB 121 AHAGFCLHASCPCPGAGVIAGPTPSQNTQCPCPPGTFSASSSSSEOCQPHRNCATGIA 180

Db 121 AHAGFCLLEHASCPPGAGVIAAGPPSONTOQPCPPGTFSSASSSSSECCOPHRNCTALGIA 180
 QY 181 LNPVSSSHDTLCTSGTGFPLSTRVPGAECERAVIDFAFODISIKRLQRLQALEAPE 240
 Db 181 LNPVSSSHDTLCTSGTGFPLSTRVPGAECERAVIDFAFODISIKRLQRLQALEAPE 240
 QY 241 GMSGPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALRVARMGCLERSVEREFLPVH 300
 Db 241 GMSGPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALRVARMGCLERSVEREFLPVH 300
 RESULT 14
 ID AAY97246 standard; Protein: 300 AA.
 AAY97246;
 AC AAY97246;
 XX
 DT 19-DEC-2000 (first entry)
 XX
 DE M68 TNF receptor related protein.
 XX
 KM M68: tumour necrosis factor; TNF; programmed cell death; apoptosis;
 KM receptor; immune response; cell differentiation; ligand; cancer;
 KM bone disease; systemic lupus erythematosus; Hashimoto's thyroiditis;
 KM Grave's disease; idiopathic myxedema; autoimmune diabetes;
 KM thrombotic thrombocytopenic purpura; multiple sclerosis;
 KM liver diseases; autoimmune gastritis; ulcerative colitis;
 KM glomerulonephritis; pulmonary fibrosis; heart failure;
 KM atherosclerosis; aplastic anaemia; myelodysplastic syndromes;
 KM osteoporosis; Alzheimer's disease; Parkinson's disease; stroke;
 KM myocardial infarction; human.
 KM
 OS Homo sapiens.
 XX
 PN W0200046247-A1.
 XX
 PD 10-AUG-2000.
 XX
 PF 04-FEB-2000; 2000MO-US03037.
 XX
 PR 05-FEB-1999; 9905-0118902.
 PR 20-DEC-1999; 9905-0172754.
 XX
 PA (MERI) MERCK & CO INC.
 XX
 PI Bai C;
 XX
 DR WPI; 2000-506066/45.
 DR N-PSDB; AAA53800, AAA53801, AAA53802.
 XX
 PT Isolated human M68 nucleic acids and proteins which are part of the
 PT tumor necrosis factor receptor (TNFR) family, useful for identifying
 PT modulators that may be used to treat various diseases e.g. cancer,
 PT osteoporosis, Alzheimer's disease
 XX
 PS Claim 1; Page 75-76; 80pp; English.
 XX
 CC The M68 protein is a member of a family of proteins which have
 CC roles in immune responses, cell death, cell proliferation and
 CC stimulation of cell differentiation. M68 lacks a transmembrane domain
 CC and is a secreted factor suggesting that it functions as a natural
 CC inhibitor for its ligand. The altered expression pattern of M68 in a
 CC multitude of tissues suggests that M68 may play a role in cancer by
 CC binding to its ligand and blocking apoptotic cell death induced by
 CC such a ligand. This anti-apoptotic role of M68 suggests that
 CC modulators of M68 will be useful in treatment of apoptosis-related
 CC diseases such as various forms of cancer and various bone disorders.
 CC M68 nucleic acids and proteins are therefore useful for treating
 CC conditions involving atypical apoptosis and for identifying
 CC modulators of M68. Modulators of M68 are useful for treatment of
 CC cancer and other diseases associated with abnormal levels of
 CC apoptosis including systemic lupus erythematosus, Hashimoto's

CC thyroiditis, Grave's disease, idiopathic myxedema, autoimmune
 CC diabetes, thrombotic thrombocytopenic purpura, multiple sclerosis,
 CC liver diseases, autoimmune gastritis, ulcerative colitis,
 CC glomerulonephritis, pulmonary fibrosis, heart failure,
 CC atherosclerosis, aplastic anaemia, myelodysplastic syndromes,
 CC osteoporosis, Alzheimer's disease, Parkinson's disease, stroke, and
 CC myocardial infarction.
 CC
 SQ Sequence 300 AA;
 Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1,4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 1 MRALGPGSLTCLVIALPALLPVPAVGAETPTYPWMDAETGERLVCAQCPTGTFVOR 60
 Db 1 MRALGPGSLTCLVIALPALLPVPAVGAETPTYPWMDAETGERLVCAQCPTGTFVOR 60
 QY 61 PCRRDSEPTTCGCPPPRHYYTQFWNYLERCRVCNVLCGEREERARACHATNRACRRTGFP 120
 Db 61 PCRRDSEPTTCGCPPPRHYYTQFWNYLERCRVCNVLCGEREERARACHATNRACRRTGFP 120
 QY 121 AHAGFCLLEHASCPPGAGVIAAGPPSONTOQPCPPGTFSSASSSSSECCOPHRNCTALGIA 180
 Db 121 AHAGFCLLEHASCPPGAGVIAAGPPSONTOQPCPPGTFSSASSSSSECCOPHRNCTALGIA 180
 QY 181 LNPVSSSHDTLCTSGTGFPLSTRVPGAECERAVIDFAFODISIKRLQRLQALEAPE 240
 Db 181 LNPVSSSHDTLCTSGTGFPLSTRVPGAECERAVIDFAFODISIKRLQRLQALEAPE 240
 QY 241 GMSGPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALRVARMGCLERSVEREFLPVH 300
 Db 241 GMSGPTPRAGRAALQKLRRRLTELLGAQDALLVRLQALRVARMGCLERSVEREFLPVH 300
 RESULT 15
 ID AAY90357 standard; Protein: 300 AA.
 AAY90357
 AC AAY90357;
 XX
 DT 04-DEC-2000 (first entry)
 XX
 DE Human tumour necrosis factor receptor-6 alpha protein sequence.
 XX
 KM Human: Tumour necrosis factor receptor 6; TNFR-6alpha; TNFR-6beta;
 KM ocular neovascularisation; solid tumour; malignancy; prostate cancer;
 KM breast cancer; colon cancer; diabetic retinopathy; microbial infection;
 KM pre-maturity macular degeneration; allergy; inflammation; tissue damage;
 KM thyroid associated ophthalmopathy; cell damage; parasitic infection;
 KM bone disease; osteoporosis; atherosclerosis; cardiovascular disease;
 KM neurodegenerative disorder; Alzheimer's disease; immune disorder;
 KM graft rejection; rheumatism; liver disease; autoimmune diabetes; asthma;
 KM psoriasis; septic shock; ulcerative colitis; therapy.
 KM
 OS Homo sapiens.
 XX
 PN W0200052028-A1.
 XX
 PD 08-SEP-2000.
 XX
 PF 03-MAR-2000; 2000MO-US05686.
 XX
 PR 04-MAR-1999; 9905-0121774.
 PR 12-MAR-1999; 9905-0124092.
 PR 27-APR-1999; 9905-0131279.
 PR 30-APR-1999; 9905-0131964.
 PR 02-AUG-1999; 9905-0146371.
 PR 01-DEC-1999; 9905-0168235.
 XX
 PA (HUMA-) HUMAN GENOME SCI INC.
 XX
 PI Gentz RL, Ni J, Ebner R, Yu G, Ruben SM, Feng P;

XX WPI: 2000-572174/53.
 DR N-PSDB; AAA37772.
 XX Nucleic acids encoding human tumour necrosis factor receptor (TNFR)
 PT proteins TNFR-6alpha and TNFR-6beta, useful for treating e.g.
 PT Alzheimer's disease, osteoporosis and graft rejection -
 XX
 PS Claim 20; Fig 1; 332pp; English.
 XX This sequence represents the human tumour necrosis factor receptor 6
 CC alpha (TNFR-6alpha) of the invention. The TNFR-6alpha and TNFR-6beta DNA
 CC and protein sequences can be used in the prevention, treatment and
 CC diagnosis of diseases associated with inappropriate TNFR expression. The
 CC nucleic acids, polypeptides, antibodies, agonists and antagonists against
 CC them may be used for the treatment of a range of conditions such as
 CC disorders associated with neovascularisation (especially ocular
 CC neovascularisation) (such as solid tumours and malignancies (e.g.
 CC prostate cancer, breast cancer and colon cancer), diabetic retinopathy
 CC and pre-maturity macular degeneration), allergies, inflammation,
 CC thyroid associated ophthalmopathy tissue/cell damage, wounds, microbial
 CC and parasitic infections, bone disease (e.g. osteoporosis),
 CC atherosclerosis, pain, cardiovascular disease (e.g. stroke),
 CC neurodegenerative disorders (e.g. Alzheimer's disease), immune
 CC disorders (e.g. graft rejection), rheumatism, liver disease,
 CC autoimmune diabetes, asthma, psoriasis, septic shock and ulcerative
 CC colitis.
 CC
 XX Sequence 300 AA:
 SQ
 Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGGLSLCLVIALPALPPAVAGVAETPTYPWRDAETGERLYCACCPGTFVQR 60
 DB 1 MRALEGGLSLCLVIALPALPPAVAGVAETPTYPWRDAETGERLYCACCPGTFVQR 60
 QY 61 PCRRDSPPTGCPCPRRHYTOFWNTLERCYNVLCGEERERARACHATHNACRCRGFF 120
 DB 61 PCRRDSPPTGCPCPRRHYTOFWNTLERCYNVLCGEERERARACHATHNACRCRGFF 120
 QY 121 AAHAGFCLHASCPRGAGVIAGTPSONTQCCPCPGTFSASSSSSECCQPHRNTALGTA 180
 DB 121 AAHAGFCLHASCPRGAGVIAGTPSONTQCCPCPGTFSASSSSSECCQPHRNTALGTA 180
 QY 181 LNVPGSSSHDPLCTSCGTFPLSTRVPGAEECEERAVIDFVARQDISIKRLQLALEAPE 240
 DB 181 LNVPGSSSHDPLCTSCGTFPLSTRVPGAEECEERAVIDFVARQDISIKRLQLALEAPE 240
 QY 241 GMSGTPRAGRAALQIKRLRRITELLAGODGALLVRLQALVARNPGLERGVRRERFLPVH 300
 DB 241 GMSGTPRAGRAALQIKRLRRITELLAGODGALLVRLQALVARNPGLERGVRRERFLPVH 300
 SQ
 RESULT 16
 AAB24395
 ID AAB24395 standard; Protein: 300 AA.
 XX
 AC AAB24395;
 XX
 DT 07-NOV-2000 (first entry)
 XX
 XX Human PRO212 protein sequence SEQ ID NO:36.
 XX
 KW Human; PRO; promotion; inhibition; angiogenesis; cardiovascularisation;
 KW diagnosis; trauma; wound; cancer; atherosclerosis; cardiac hypertrophy;
 KW angiogenic; proliferative; cardiac; cardiovascular; antiatherosclerotic;
 KW cytoskeletal; gene therapy; vaccine.
 XX
 OS Homo sapiens.
 XX
 PN WO200032221-A2.

XX 08-JUN-2000.
 PD 30-NOV-1999; 99WO-US28313.
 XX
 XX 01-DEC-1998; 98WO-US25108.
 XX 16-DEC-1998; 98US-0112850.
 PR 12-JAN-1999; 99US-0115554.
 PR 08-MAR-1999; 99WO-US05028.
 PR 12-MAR-1999; 99US-0123957.
 PR 28-APR-1999; 99US-0131445.
 PR 14-MAY-1999; 99US-0134287.
 PR 02-JUN-1999; 99WO-US12252.
 PR 23-JUN-1999; 99US-0141037.
 PR 20-JUL-1999; 99US-0144758.
 PR 26-JUL-1999; 99US-0145698.
 PR 01-SEP-1999; 99WO-US20111.
 PR 08-SEP-1999; 99WO-US20594.
 PR 13-SEP-1999; 99WO-US20944.
 PR 15-SEP-1999; 99WO-US21090.
 PR 15-SEP-1999; 99WO-US21547.
 PR 05-OCT-1999; 99WO-US23089.
 PR 29-OCT-1999; 99US-0162506.
 XX
 PA (GENENTECH INC.
 XX
 PI Ashkenazi AJ, Baker KP, Ferrara N, Gerber H, Hillan KJ, Goddard A;
 PI Godowski PJ, Gurney AL, Klein RD, Kuo SS, Paoni NF, Smith V;
 PI Watanabe CK, Williams PM, Wood WI;
 XX
 DR WPI: 2000-412154/35.
 N-PSDB; AAA77537.
 XX
 XX Nucleic acids encoding PRO polypeptides useful for preventing,
 PT diagnosing and treating disorders in cardiovascular, endothelial or
 PT angiogenic disorders in mammals -
 XX
 PS Claim 72; Fig 16; 315pp; English.
 XX
 CC The present invention describes nucleic acids encoding PRO polypeptides
 CC useful for preventing, diagnosing and treating disorders in mammals by
 CC cardiovascular, endothelial or angiogenic disorder in mammals by
 CC modulating cell proliferation, angiogenesis and cardiovascularisation,
 CC and for identifying agonists and antagonists of these processes. The
 CC nucleic acids and the proteins they encode may be used in the
 CC prevention, treatment and diagnosis of diseases associated with
 CC inappropriate PRO expression such as cardiovascular, endothelial or
 CC angiogenic disorders in mammals (e.g. atherosclerosis, cancers and
 CC cardiac hypertrophy). For example, the nucleic acids (NCs) and vectors
 CC containing them and the PRO polypeptide may be used to treat disorders
 CC associated with decreased PRO expression. AAA77510 to AAA77721 and
 CC AAB24388 to AAB24435 represent nucleotide and protein sequences used in
 CC the exemplification of the present invention.
 XX
 SQ Sequence 300 AA:
 Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGGLSLCLVIALPALPPAVAGVAETPTYPWRDAETGERLYCACCPGTFVQR 60
 DB 1 MRALEGGLSLCLVIALPALPPAVAGVAETPTYPWRDAETGERLYCACCPGTFVQR 60
 QY 61 PCRRDSPPTGCPCPRRHYTOFWNTLERCYNVLCGEERERARACHATHNACRCRGFF 120
 DB 61 PCRRDSPPTGCPCPRRHYTOFWNTLERCYNVLCGEERERARACHATHNACRCRGFF 120
 QY 121 AAHAGFCLHASCPRGAGVIAGTPSONTQCCPCPGTFSASSSSSECCQPHRNTALGTA 180
 DB 121 AAHAGFCLHASCPRGAGVIAGTPSONTQCCPCPGTFSASSSSSECCQPHRNTALGTA 180
 QY 181 LNVPGSSSHDPLCTSCGTFPLSTRVPGAEECEERAVIDFVARQDISIKRLQLALEAPE 240
 DB 181 LNVPGSSSHDPLCTSCGTFPLSTRVPGAEECEERAVIDFVARQDISIKRLQLALEAPE 240
 QY

```

Db      181 LNPVGSSSHDTLCTSGTGFPLSTRVGAECERAVIDFAFDISIKRLQRLQALEAPE 240
QY      241 GMGPTPRAGAAQLKLRRLTELLGAQDALLVRLQALRVARMGERSVEREFLPVH 300
        241 GMGPTPRAGAAQLKLRRLTELLGAQDALLVRLQALRVARMGERSVEREFLPVH 300

RESULT 17
ID      AAY96596 standard; Protein; 300 AA.
AC      AAY96596;
DE      26-SEP-2000 (first entry)
XX      Human FLINT.
KW      FLINT; osteoprotegerin 3; OPG3; tumour necrosis factor receptor; TNFR;
KW      FasL; LIGHT; apoptosis; pro-inflammatory; hepatotropic; vasotropic;
KW      anti-diabetic; anti-anaemic; neuroprotective; anti-ulcer; cytostatic;
KW      anti-inflammatory; antibacterial; immunosuppressive.
XX      Homo sapiens.
OS
FH      Key
FT      Peptide
FT      Protein
        Location/Qualifiers
        1..29
        /label= Signal_peptide
        30..300
        /label= Mature_Protein
        WO200037094-A2.
XX      PD
        29-JUN-2000.
XX      PF
        21-DEC-1999; 99WO-US30734.
XX      PR
        22-DEC-1998; 98US-0113407.
        30-MAR-1999; 99WO-US06797.
        20-OCT-1999; 99US-0172339.
XX      PA
        (ELIL ) LILLY & CO ELI.
XX      PI
        Cohen FU, Posada JA, Wierda D;
        WPI: 2000-475441/41.
        N-PSDB; AAA51075.
XX      DR
        Use of mature FLINT for treating e.g. acute respiratory distress
        syndrome, ulcerative colitis or ischemic injury during organ
        transplantation
XX      PT
        Example 7; Fig 1A-B; 125pp; English.
XX      PS
        Human FLINT (also known as osteoprotegerin 3) is a new tumour necrosis
        factor receptor (TNFR) superfamily member, which binds FasL and LIGHT and
        prevents FasL-Fas interaction. Mature FLINT (mFLINT) inhibits FasL-Fas
        mediated apoptotic and pro-inflammatory activity. mFLINT is useful for
        treating acute respiratory distress syndrome, treating or inhibiting
        ulcerative colitis, inhibiting ischemic injury during organ
        transplantation or for organ preservation during transplantation. mFLINT
        can also be used to treat acute liver failure, inflammation of the liver,
        abnormal (hepatocyte) apoptosis, sepsis, disorders associated with
        inflammation, hepatitis, ischemia, hypercoagulation or reperfusion,
        damage to a cardiac myocyte resulting from abnormal myocardial ischemia,
        Type I diabetes, cancer, damage to an innocent bystander tissue induced
        by a chemotherapeutic or therapeutic irradiation, aplastic anemias,
        myelodysplastic syndromes and pancytopenic conditions.
XX      CC
        Sequence 300 AA:
XX

```

```

Matches 300; Conservative 0; Mismatches 0; Indels 0; Caps 0;
QY      1 MRALGPGSLTLCLVIALPALPEVPAVGVAEPTPTVPMRDATGERTVCAQCPGTFFVOR 60
        1 MRALGPGSLTLCLVIALPALPEVPAVGVAEPTPTVPMRDATGERTVCAQCPGTFFVOR 60
Db      61 PCRDSPTTCGCPPPRHYYTFMWYLERCRYCNVLCGEREEARACHATNRACRCRTGFF 120
        61 PCRDSPTTCGCPPPRHYYTFMWYLERCRYCNVLCGEREEARACHATNRACRCRTGFF 120
Db      61 PCRDSPTTCGCPPPRHYYTFMWYLERCRYCNVLCGEREEARACHATNRACRCRTGFF 120
QY      121 AHAGFCLHNASCPGAGVIVAGTSPQNTQCQCPGPFSSASSSSDQCPHRRCTLGLA 180
        121 AHAGFCLHNASCPGAGVIVAGTSPQNTQCQCPGPFSSASSSSDQCPHRRCTLGLA 180
Db      121 AHAGFCLHNASCPGAGVIVAGTSPQNTQCQCPGPFSSASSSSDQCPHRRCTLGLA 180
QY      181 LNPVGSSSHDTLCTSGTGFPLSTRVGAECERAVIDFAFDISIKRLQRLQALEAPE 240
        181 LNPVGSSSHDTLCTSGTGFPLSTRVGAECERAVIDFAFDISIKRLQRLQALEAPE 240
Db      181 LNPVGSSSHDTLCTSGTGFPLSTRVGAECERAVIDFAFDISIKRLQRLQALEAPE 240
QY      241 GMGPTPRAGAAQLKLRRLTELLGAQDALLVRLQALRVARMGERSVEREFLPVH 300
        241 GMGPTPRAGAAQLKLRRLTELLGAQDALLVRLQALRVARMGERSVEREFLPVH 300
Db      241 GMGPTPRAGAAQLKLRRLTELLGAQDALLVRLQALRVARMGERSVEREFLPVH 300

RESULT 18
ID      AAE03568 standard; Protein; 300 AA.
AC      AAE03568;
DE      04-AUG-2001 (first entry)
XX      DE
        Human native fas ligand inhibitory protein (FLINT).
XX      KW
        Human: fas ligand inhibitory protein; FLINT; acute lung injury; ALI;
        TNFR; tumour necrosis factor receptor protein; ulcerative colitis; ARDS;
        acute respiratory distress syndrome; pulmonary fibrosis; PF; therapy;
        chronic obstructive pulmonary disease; COPD; acute lung injury; goitre;
        rheumatoid arthritis; fibroproliferative lung disease; Ischemia; sepsis;
        fibrotic lung disease; human immunodeficiency virus; HIV; osteoporosis;
        chronic renal failure; graft-vs-host disease; cutaneous inflammation;
        vascular leak syndrome; Helicobacter pylori infection; atherosclerosis;
        insulin dependent diabetes mellitus (IDDM); inflammatory bowel disease;
        Crohn's disease; pancreatitis; cancer; autoimmune disease; psoriasis;
        Down's syndrome; multiple sclerosis; cytostatic; neutrotropic;
        neuroprotective; vasotropic.
XX      KW
        Homo sapiens.
XX      OS
FH      Key
FT      Peptide
FT      Protein
        Location/Qualifiers
        1..29
        /label= Signal_peptide
        30..300
        /note= "Mature human FLINT"
        203
        Modified-site
        /note= "O-linked glycosylation site"
        245
        Modified-site
        /note= "O-linked glycosylation site"
        247..248
        Cleavage-site
        /note= "Proteolytic cleavage"
        WO200142463-A1.
XX      PD
        14-JUN-2001.
XX      PF
        29-NOV-2000; 2000MO-US30166.
XX      PR
        07-DEC-1999; 99US-0169367.
        07-DEC-1999; 99US-0169381.
        07-DEC-1999; 99US-0169412.
        23-MAR-2000; 2000US-0191430.
XX      PA
        (ELIL ) LILLY & CO ELI.
XX

```

Query Match 100.0%; Score 1634; DB 21; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;

PI Lu J, Witcher DR;
 XX MPI; 2001-381684/40.
 XX
 PT New FLINT polypeptide for treating and/or preventing acute lung injury,
 PT acute respiratory distress syndrome, ulcerative colitis, and
 PT graft-versus-host disease, comprises O-linked or N-linked
 PT oligosaccharides -
 XX
 PS Example 2: Page 54-55; 60pp; English.
 XX
 CC The present sequence is human native fas ligand inhibitory protein
 CC (FLINT). FLINT, a homologue of tumour necrosis factor receptor
 CC protein (TNFR), binds fas ligand (FasL) and thereby preventing the
 CC interaction of FasL with fas. FLINT comprising O-linked or N-linked
 CC oligosaccharides is useful for preventing or treating acute lung injury
 CC (ALI), acute respiratory distress syndrome (ARDS), ulcerative colitis,
 CC chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis (PF),
 CC to facilitate organ preservation for transplantation and to inhibit T
 CC lymphocyte activation. FLINT is useful for treating and/or preventing
 CC diseases such as rheumatoid arthritis, fibropoliferative lung disease,
 CC fibrotic lung disease, acute lung injury, human immunodeficiency virus
 CC (HIV), ischaemia, brain trauma/injury, chronic renal failure, graft-vs-
 CC host disease, cutaneous inflammation, vascular leak syndrome,
 CC Helicobacter pylori infection, goitre, atherosclerosis, insulin dependent
 CC diabetes mellitus (IDDM), osteoporosis, inflammatory bowel disease,
 CC Crohn's disease, sepsis, pancreatitis, cancer, autoimmune disease such as
 CC psoriasis, Down's syndrome, and multiple sclerosis.
 CC
 SO Sequence 300 AA;
 Query Match 100.0%; Score 1634; DB 22; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1,4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGELSLCLVLAIPALPPAVAGVAETPTYPWRDAETGERLYCAACPGTFVQR 60
 DB 1 MRALEGELSLCLVLAIPALPPAVAGVAETPTYPWRDAETGERLYCAACPGTFVQR 60
 QY 61 PCRRDPTTCGPPRRHTQFWNTLERCYNVLCGEREEERARACHAHNACRCRTGFF 120
 DB 61 PCRRDPTTCGPPRRHTQFWNTLERCYNVLCGEREEERARACHAHNACRCRTGFF 120
 QY 121 AHAGFCLHASCPCGAGVIAPGTPSQNTQCCPPGTFSSASSSSSEQCQPHRNCATGLA 180
 DB 121 AHAGFCLHASCPCGAGVIAPGTPSQNTQCCPPGTFSSASSSSSEQCQPHRNCATGLA 180
 QY 181 LNVPGSSSHDTLCTSCGFPILSTRVPGAEECEERAVIDVFADODISIKRLQRLQALEAPE 240
 DB 181 LNVPGSSSHDTLCTSCGFPILSTRVPGAEECEERAVIDVFADODISIKRLQRLQALEAPE 240
 QY 241 GWGPTPRAGRAALQDKLRRLTELLGADGALLVRLQALVAVARMPGLERSVRETFPVH 300
 DB 241 GWGPTPRAGRAALQDKLRRLTELLGADGALLVRLQALVAVARMPGLERSVRETFPVH 300

RESULT 19
 AAB74466
 ID AAB74466 standard; protein: 300 AA.
 XX
 AC AAB74466;
 XX
 DT 30-MAY-2001 (first entry)
 XX
 DE Human FLINT native protein.
 XX
 KW Human; FLINT; Fas ligand inhibitory protein; analogue; apoptosis;
 KW inflammatory disease.
 XX
 OS Homo sapiens.
 XX
 FH Key Location/Qualifiers
 FT Misc-difference 182

PT /note= "encoded by AT?"
 FT Misc-difference 243
 FT /note= "encoded by GCT"
 XX
 PN WO200118202-A2.
 XX
 PD 15-MAR-2001.
 XX
 PF 31-AUG-2000; 2000WO-US20806.
 XX
 PR 10-SEP-1999; 99US-0153433.
 XX
 PA (ELIL) LILLY & CO ELI.
 XX
 PI Atkinson PR, Tian Y, Witcher DR;
 XX
 DR MPI; 2001-257796/26.
 XX
 PS N-PSDB; AAF77696.
 XX
 CC The present invention describes a composition comprising a divalent metal
 CC cation associated with a protease resistant Fas ligand inhibitory protein
 CC (FLINT) analogue. The composition is useful in the treatment of diseases
 CC associated with Fas binding to its ligand, such as acute liver failure,
 CC inflammatory diseases, cerebral ischaemia and apoptosis. The present
 CC sequence is the native FLINT protein.
 CC
 SO Sequence 300 AA;
 Query Match 100.0%; Score 1634; DB 22; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1,4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGELSLCLVLAIPALPPAVAGVAETPTYPWRDAETGERLYCAACPGTFVQR 60
 DB 1 MRALEGELSLCLVLAIPALPPAVAGVAETPTYPWRDAETGERLYCAACPGTFVQR 60
 QY 61 PCRRDPTTCGPPRRHTQFWNTLERCYNVLCGEREEERARACHAHNACRCRTGFF 120
 DB 61 PCRRDPTTCGPPRRHTQFWNTLERCYNVLCGEREEERARACHAHNACRCRTGFF 120
 QY 121 AHAGFCLHASCPCGAGVIAPGTPSQNTQCCPPGTFSSASSSSSEQCQPHRNCATGLA 180
 DB 121 AHAGFCLHASCPCGAGVIAPGTPSQNTQCCPPGTFSSASSSSSEQCQPHRNCATGLA 180
 QY 181 LNVPGSSSHDTLCTSCGFPILSTRVPGAEECEERAVIDVFADODISIKRLQRLQALEAPE 240
 DB 181 LNVPGSSSHDTLCTSCGFPILSTRVPGAEECEERAVIDVFADODISIKRLQRLQALEAPE 240
 QY 241 GWGPTPRAGRAALQDKLRRLTELLGADGALLVRLQALVAVARMPGLERSVRETFPVH 300
 DB 241 GWGPTPRAGRAALQDKLRRLTELLGADGALLVRLQALVAVARMPGLERSVRETFPVH 300

RESULT 20
 AAB71754
 ID AAB71754 standard; Protein: 300 AA.
 XX
 AC AAB71754;
 XX
 DT 02-MAY-2001 (first entry)
 XX
 DE Human NTR3.
 XX
 KW Human; NTR3; tumour necrosis factor receptor; TNF receptor; anti-HIV;
 KW anti-nausea; immunosuppressive; antidiabetic; antiviral; antibacterial;
 KW cytostatic; neuroprotective; antiinflammatory; anorectic; vasotrophic;
 KW antirheumatoid; antiarthritic; cerebroprotective; tuberculostatic;

KW gene therapy; cancer; blood disorder; brain disorder; autoimmune disease;
 XX infection.
 XX
 OS Homo sapiens.
 XX
 PN W0200110908-A1.
 XX
 PD 15-FEB-2001.
 XX
 PF 02-AUG-2000; 2000WO-US21287.
 XX
 PR 04-AUG-1999; 99US-0147297.
 XX
 PA (AMGE-) AMGEN INC.
 XX
 PI Hsu H;
 XX
 DR WPI; 2001-191521/19.
 DR N-PSDB; AAF62705.
 XX
 PT New tumor necrosis factor receptor, NTR3, useful for treating cancers,
 PT stroke, anemia, obesity, rheumatoid arthritis and transplantation
 PT rejection -
 PS
 PS Claim 14; Page 129-130, 135pp. English.
 XX
 CC The present sequence is the tumour necrosis factor (TNF) receptor
 CC polypeptide NTR3. The NTR3 polynucleotides and polypeptides are useful
 CC for treating diseases such as acquired-immunodeficiency syndrome (AIDS),
 CC anaemia, autoimmune diseases, cachexia, cancer, cerebral malaria,
 CC diabetes mellitus, disseminated intravascular coagulopathy, erythroid
 CC sick syndrome, haemorrhagic shock, hepatitis, insulin resistance,
 CC leprosy, leukaemia, meningitis, multiple sclerosis, myocardial ischaemia,
 CC obesity, rejection of transplanted organs, rheumatoid arthritis, septic
 CC shock syndrome, stroke, adult respiratory distress syndrome (ARDS),
 CC tuberculosis, and a number of viral diseases. The NTR3 polypeptide is
 CC useful for identifying or developing new (ant)agonists of NTR3. It may
 CC be used as an immunogen to which antibodies may be raised. NTR3 nucleic
 CC acid molecules may be useful as hybridisation probes in diagnostic assays
 CC to test, either qualitatively or quantitatively, for the presence of an
 CC NTR3 DNA or corresponding RNA in mammalian tissue or bodily fluid
 CC samples.
 CC
 CC
 SQ Sequence 300 AA;
 Query Match 100.0%; Score 1634; DB 22; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALGGLSLCLIVLALPALLPVAVRGVAETPTTWRDAETGERLVCAQCPPTGVQR 60
 DB 1 MRALGGLSLCLIVLALPALLPVAVRGVAETPTTWRDAETGERLVCAQCPPTGVQR 60
 QY 61 PCRDSPTTGGPCPPRRHYTFWMNLERCRVCNVLCGRREEARACHTHRACCPCTGFF 120
 DB 61 PCRDSPTTGGPCPPRRHYTFWMNLERCRVCNVLCGRREEARACHTHRACCPCTGFF 120
 QY 121 AHAGFCLERHASCPCGACVIAPTGPTSONTOCCPCPPTGTFSSSSSSSECCQPHRNCATGALA 180
 DB 121 AHAGFCLERHASCPCGACVIAPTGPTSONTOCCPCPPTGTFSSSSSSSECCQPHRNCATGALA 180
 QY 121 AHAGFCLERHASCPCGACVIAPTGPTSONTOCCPCPPTGTFSSSSSSSECCQPHRNCATGALA 180
 DB 121 AHAGFCLERHASCPCGACVIAPTGPTSONTOCCPCPPTGTFSSSSSSSECCQPHRNCATGALA 180
 QY 181 LNPVGSSSHDTLCTSCGFPULSTRVPGAECECERAVIDFVAFODISIKRLQRLQALTAPE 240
 DB 181 LNPVGSSSHDTLCTSCGFPULSTRVPGAECECERAVIDFVAFODISIKRLQRLQALTAPE 240
 QY 241 GMPPTPRAGRAALQIKRRRLTELGGODGALLVRLQALRVARNMGLERSVRRRLPVH 300
 DB 241 GMPPTPRAGRAALQIKRRRLTELGGODGALLVRLQALRVARNMGLERSVRRRLPVH 300

XX AAB48161;
 AC
 XX 02-APR-2001 (first entry)
 DT
 XX Human PRO212 polypeptide.
 DE
 XX PRO212; PRO326; PRO1016; neoplastic; cell growth; tumour; cancer;
 KW breast; ovarian; renal; colorectal; uterine; prostate; lung; melanoma;
 KW central nervous system; leukemia; antitumor; cytostatic.
 XX
 OS Homo sapiens.
 XX
 FH Key
 FH Peptide
 FT 1..23 Location/Qualifiers
 FT /note= "signal peptide"
 FT 24..300
 FT Protein
 FT /note= "mature protein"
 FT 28..37
 FT Modified-site
 FT /note= "tyrosine kinase phosphorylation site"
 FT 63..67
 FT /note= "cAMP and cGMP-dependent protein kinase phosphorylation sites"
 FT
 FT Domain
 FT 125..145
 FT /note= "transmembrane domain"
 FT 163..167
 FT Modified-site
 FT /note= "casein kinase II phosphorylation site"
 FT 173..177
 FT Modified-site
 FT /note= "aen is N-glycosylated"
 FT 156..162
 FT Modified-site
 FT /note= "N-myristoylation"
 FT 178..184
 FT Modified-site
 FT /note= "N-myristoylation"
 FT 187..191
 FT Modified-site
 FT /note= "casein kinase II phosphorylation site"
 FT 207..213
 FT Modified-site
 FT /note= "N-myristoylation"
 FT 259..263
 FT Modified-site
 FT /note= "cAMP and cGMP-dependent protein kinase phosphorylation sites"
 FT 266..272
 FT Modified-site
 FT /note= "N-myristoylation"
 FT 287..293
 FT Modified-site
 FT /note= "N-myristoylation"
 FT 291..295
 FT Modified-site
 FT /note= "casein kinase II phosphorylation site"
 PN W0200075316-A1.
 XX
 XX 14-DEC-2000.
 PD
 XX 20-DEC-1999; 99WO-US30911.
 PF
 XX 02-JUN-1999; 99WO-US12252.
 PR 23-JUN-1999; 99US-0141037.
 PR 07-JUL-1999; 99US-0143048.
 PR 15-SEP-1999; 99WO-US21090.
 PR 15-SEP-1999; 99WO-US21547.
 PR 30-NOV-1999; 99WO-US28313.
 XX
 PA (GETH) GENENTECH INC.
 XX
 PI Ashkenazi AV, Goddard A, Gurney AL, Hillan K, Napier M, Wood WI;
 XX
 DR WPI; 2001-050025/06.
 DR N-PSDB; AAC84421.
 XX
 PT Composition for inhibiting neoplastic cell growth and treating a tumor
 PT or cancer, comprises novel PRO212, PRO326, PRO1016 polypeptides or
 PT agonists of them
 XX
 PS Claim 31; Fig 2; 116pp. English.

CC The invention provides PRO212, PRO326 or PRO1016 polypeptides that can be
 CC used for the inhibition of neoplastic cell growth and for treating
 CC tumours. The PRO polypeptides can be expressed by standard recombinant
 CC methodology. The PRO polypeptides or their agonists are useful for
 CC inhibition of neoplastic cell growth and for treating tumours, cancers
 CC such as breast, ovarian, renal, colorectal, uterine, prostate, lung,
 CC bladder or central nervous system cancers or melanoma and leukemia. The
 CC present sequence represents the human PRO212 polypeptide.

XX Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 22; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1,4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGGSLILCLIVLALPALPPAVRGVAETTYMRAETGERLYVCAACPGPTGYOR 60
 DB 1 MRALEGGSLILCLIVLALPALPPAVRGVAETTYMRAETGERLYVCAACPGPTGYOR 60
 QY 61 PCRDSPTTCGPPRRHYTOFWNYLERCRCNVLCGEREEBARACHATHNRACRCRTGFF 120
 DB 61 PCRDSPTTCGPPRRHYTOFWNYLERCRCNVLCGEREEBARACHATHNRACRCRTGFF 120
 QY 121 AHAGFCLHASCPRGAGVIAPGTPSQNTQCCPPTGTFSSSSSECCOPHRNCTALGIA 180
 DB 121 AHAGFCLHASCPRGAGVIAPGTPSQNTQCCPPTGTFSSSSSECCOPHRNCTALGIA 180
 QY 181 LNVGSSSHDTLCTSCGFPILSTRVPGAEBCERAVIDFVAFODISIKRLRLQALAEPE 240
 DB 181 LNVGSSSHDTLCTSCGFPILSTRVPGAEBCERAVIDFVAFODISIKRLRLQALAEPE 240
 QY 241 GMGFTPRAGRALQKLRRLTELLGADGALLVRLQALVAMPGLERSVREPRFPVH 300
 DB 241 GMGFTPRAGRALQKLRRLTELLGADGALLVRLQALVAMPGLERSVREPRFPVH 300

RESULT 22
 AAB50903
 XX AAB50903 standard; Protein: 300 AA.
 AC AAB50903;
 XX
 DT 21-MAR-2001 (first entry)
 XX
 DE Human PRO212 protein.
 XX
 KW Human; PRO; antiinflammatory; dermatological; antiarthritic;
 KW antirheumatic; cardiant; antianaemic; immunosuppressive; antithyroid;
 KW antidiabetic; noctropic; neuroprotective; hepatotropic; virucide;
 KW antiallergic; antiasthmatic; immune related disorder;
 KW hepatobiliary disease; autoimmune disease; allergy.
 XX
 OS Homo sapiens.
 XX
 FN WO200073452-A2.
 XX
 PD 07-DEC-2000.
 XX
 PE 02-JUN-2000; 2000WO-US15264.
 XX
 PR 02-JUN-1999; 99WO-US12252.
 PR 20-JUL-1999; 99US-0144732.
 PR 20-JUL-1999; 99US-0144732.
 PR 28-JUL-1999; 99US-0146232.
 PR 01-SEP-1999; 99WO-US20111.
 PR 15-SEP-1999; 99WO-US21090.
 PR 15-SEP-1999; 99WO-US21347.
 PR 29-OCT-1999; 99US-0162506.
 PR 30-NOV-1999; 99WO-US28313.
 PR 01-DEC-1999; 99WO-US28634.
 PR 09-DEC-1999; 99US-0170262.
 PR 20-DEC-1999; 99WO-US30911.
 PR 03-JAN-2000; 2000WO-US00219.

PR 06-JAN-2000; 2000WO-US00376.
 PR 11-FEB-2000; 2000WO-US03565.
 PR 18-FEB-2000; 2000WO-US04341.
 PR 18-FEB-2000; 2000WO-US04342.
 PR 22-FEB-2000; 2000WO-US04414.
 PR 24-FEB-2000; 2000WO-US04914.
 PR 15-MAR-2000; 2000WO-US06884.
 PR 20-MAR-2000; 2000WO-US07377.
 PR 21-MAR-2000; 2000WO-US07532.
 PR 30-MAR-2000; 2000WO-US08439.
 PR 17-MAY-2000; 2000WO-US13705.
 PR 22-MAY-2000; 2000WO-US14042.

PA (GETH) GENENTECH INC.

XX Ashkenazi AJ, Baker KP, Chan B, Goddard A, Godowski PJ, Gurney AL;
 PI Hebert C, Henzel W, Kabakoff RC, Shelton DL, Tunas D, Watanabe CK;
 PI Wood WI;

XX WPI: 2001-025253/03.
 DR N-PSDB: AAC91462.

PT Thirty three nucleic acids encoding PRO polypeptides which are useful
 PT in the diagnosis and treatment of immune related disorders, e.g.
 PT systemic lupus erythematosus, rheumatoid arthritis, osteoarthritis,
 PT thyroiditis and diabetes mellitus -

XX Claim 58; Fig 4; 218pp; English.

XX The present sequence is one of thirty three novel PRO polypeptides.
 CC The PRO polypeptides, anti-PRO antibodies, agonists and
 CC antagonists are useful for treating and diagnosing immune related
 CC disorders such as systemic lupus erythematosus, rheumatoid arthritis,
 CC osteoarthritis, juvenile chronic inflammatory myopathies, Sjogren's
 CC syndrome, systemic sclerosis, idiopathic chronic hepatitis, primary
 CC biliary cirrhosis, autoimmune hemolytic anemia, autoimmune haemolytic
 CC anemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus,
 CC immune-mediated renal disease, demyelinating diseases of the central
 CC and peripheral nervous systems (such as multiple sclerosis, idiopathic
 CC demyelinating polyneuropathy or Guillain-Barre syndrome, and chronic
 CC inflammatory demyelinating polyneuropathy), hepatobiliary diseases
 CC (such as infectious, autoimmune chronic active hepatitis, primary
 CC biliary cirrhosis, granulomatous hepatitis and sclerosing cholangitis),
 CC inflammatory bowel disease, gluten-sensitive enteropathy and Whipple's
 CC disease, autoimmune or immune-mediated skin diseases (such as bullous
 CC skin diseases, erythema multiforme, contact dermatitis, psoriasis),
 CC allergic diseases such as asthma, allergic rhinitis, atopic dermatitis,
 CC food hypersensitivity and urticaria), immunological diseases of the
 CC lung (such as eosinophilic pneumonias, idiopathic pulmonary fibrosis
 CC and hypersensitivity pneumonitis), transplantation associated diseases
 CC including graft rejection and graft-versus-host diseases.
 XX

SO Sequence 300 AA;

Query Match 100.0%; Score 1634; DB 22; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1,4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEGGSLILCLIVLALPALPPAVRGVAETTYMRAETGERLYVCAACPGPTGYOR 60
 DB 1 MRALEGGSLILCLIVLALPALPPAVRGVAETTYMRAETGERLYVCAACPGPTGYOR 60
 QY 61 PCRDSPTTCGPPRRHYTOFWNYLERCRCNVLCGEREEBARACHATHNRACRCRTGFF 120
 DB 61 PCRDSPTTCGPPRRHYTOFWNYLERCRCNVLCGEREEBARACHATHNRACRCRTGFF 120
 QY 121 AHAGFCLHASCPRGAGVIAPGTPSQNTQCCPPTGTFSSSSSECCOPHRNCTALGIA 180
 DB 121 AHAGFCLHASCPRGAGVIAPGTPSQNTQCCPPTGTFSSSSSECCOPHRNCTALGIA 180
 QY 181 LNVGSSSHDTLCTSCGFPILSTRVPGAEBCERAVIDFVAFODISIKRLRLQALAEPE 240
 DB 181 LNVGSSSHDTLCTSCGFPILSTRVPGAEBCERAVIDFVAFODISIKRLRLQALAEPE 240

QY 241 GMGPTRAGRAALQQLKRLRRLTELLGADGALLVRLQALRVARMGLESVERERFLPVH 300
 DB 241 GMGPTRAGRAALQQLKRLRRLTELLGADGALLVRLQALRVARMGLESVERERFLPVH 300

RESULT 23
 AAE14579
 ID AAE14579 standard; Protein; 300 AA.
 AC AAE14579;
 DT 01-JUL-2002 (first entry)
 DE Human native FLINT precursor protein.
 XX
 FLINT: FAS ligand inhibitory protein; pulmonary; lung; apoptosis;
 KW organ failure; liver; kidney; pancreas; inflammatory disease;
 KW neutrophil; sepsis; acute respiratory distress syndrome;
 KW acute lung injury; systemic inflammatory response syndrome; SIRS;
 KW multiple organ dysfunction; MODS; human.
 XX
 OS Homo sapiens.
 FH Key Location/Qualifiers
 FT Peptide 1..29
 FT /label= Leader_peptide
 FT Protein 30..300
 FT /label= Mature_FLINT
 XX
 PN WO200209668-A2.
 XX
 PD 07-FEB-2002.
 PD 20-JUL-2001; 2001MO-US21105.
 PF 02-AUG-2000; 2000US-222476P.
 PR
 XX
 PA (ELIL) LILLY & CO ELI.
 XX
 PI Micanovic R, Wltscher DR;
 XX
 DR WPI; 2002-206149/26.
 XX
 PT Administering FLINT (FAS ligand inhibitory protein) or FLINT analog,
 PT useful for treating e.g. sepsis or respiratory distress syndrome,
 PT involves pulmonary administration of a therapeutic amount of the FLINT
 PT or FLINT analog -
 XX
 PS Disclosure; Page 31-32; 35pp; English.
 XX
 CC The invention relates to a new method of administering FLINT
 CC (FAS ligand inhibitory protein) or FLINT analog that involves pulmonary
 CC administration of a therapeutic amount of the FLINT or FLINT analog.
 CC The method enables systemic absorption of FLINT through lungs and
 CC significantly reduces or eliminates the need for administering FLINT by
 CC injection or other routes of administration. The method is useful in
 CC treating disorders related to enhanced apoptosis (e.g. organ failure
 CC in liver, kidneys and pancreas) and inflammatory diseases associated with
 CC neutrophil activation (e.g. sepsis, acute respiratory distress syndrome,
 CC acute lung injury, systemic inflammatory response syndrome (SIRS) and
 CC multiple organ dysfunction (MODS)). The method maintains the pain
 CC and discomfort of injection methods. The present sequence is human
 CC native FLINT precursor protein.
 CC
 SO Sequence 300 AA:

Query Match 100.0%; Score 1634; DB 23; Length 300;
 Best Local Similarity 100.0%; Pred. No. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MRALEPGSLCLCVIALPALLPVPAVGVAEPTPTVPMRDAETGERLVCAQCPRPGTFVOR 60
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

DB 1 MRALEPGSLCLCVIALPALLPVPAVGVAEPTPTVPMRDAETGERLVCAQCPRPGTFVOR 60
 QY 61 PCRDSPTTGGPCPPRRHYTOFMVYLERCRVNCVCGREBEARACHATHNRACRCRTGFF 120
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 DB 61 PCRDSPTTGGPCPPRRHYTOFMVYLERCRVNCVCGREBEARACHATHNRACRCRTGFF 120
 QY 121 AHAGFCLERHASCPPGAGVIAPGTPSONTOCQPCPGTFSASSSSSECCQPHNRCTALGTA 180
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 DB 121 AHAGFCLERHASCPPGAGVIAPGTPSONTOCQPCPGTFSASSSSSECCQPHNRCTALGTA 180
 QY 181 LNPVGSSSHDTCTGCTGFPPLSTRVPGAECERCAVIDFAFODISIKRLQRLQALEAPE 240
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 DB 181 LNPVGSSSHDTCTGCTGFPPLSTRVPGAECERCAVIDFAFODISIKRLQRLQALEAPE 240
 QY 241 GMGPTRAGRAALQQLKRLRRLTELLGADGALLVRLQALRVARMGLESVERERFLPVH 300
 DB 241 GMGPTRAGRAALQQLKRLRRLTELLGADGALLVRLQALRVARMGLESVERERFLPVH 300

RESULT 24
 AAE20848
 ID AAE20848 standard; Protein; 300 AA.
 AC AAE20848;
 DT 01-JUL-2002 (first entry)
 DE Human tumour necrosis factor receptor (TNFR)-6alpha protein.
 XX
 KW Human: tumour necrosis factor receptor; "TNFR-6alpha; TNFR-6beta; therapy;
 KW immune system-related disorder; inflammatory disease; immunosuppressive;
 KW bowel disease; encephalitis; atherosclerosis; gastrointestinal-Gen;
 KW autoimmune disease; systemic lupus erythematosus; rheumatoid arthritis;
 KW multiple sclerosis; Crohn's disease; autoimmune encephalitis; allergy;
 KW graft versus host disease; GVHD; antiinflammatory; psoriasis; arthritis;
 KW neuroprotective; antiarteriosclerotic; dermatological; asthma; receptor.
 XX
 OS Homo sapiens.
 FH Key Location/Qualifiers
 FT Peptide 1..30
 FT /label= Signal_peptide
 FT Protein 31..300
 FT /note= "Human TNFR-6alpha protein"
 FT Domain 31..283
 FT /note= "Extracellular domain"
 FT Region 31..46
 FT /note= "Antigenic region"
 FT Region 57..117
 FT /note= "Antigenic region"
 FT Region 132..175
 FT /note= "Antigenic region"
 FT Region 185..194
 FT /note= "Antigenic region"
 FT Region 205..217
 FT /note= "Antigenic region"
 FT Region 239..264
 FT /note= "Antigenic region"
 FT Region 283..298
 FT /note= "Antigenic region"
 PN WO200218622-A2.
 XX
 PD 07-MAR-2002.
 XX
 PD 24-AUG-2001; 2001MO-US26396.
 PF 25-AUG-2000; 2000US-227598P.
 PR 21-NOV-2000; 2000US-252131P.
 PR 06-JUL-2001; 2001US-303224P.
 XX
 PA (HUMA-) HUMAN GENOME SCI INC.

PI Gentz RL, Edner R, Yu G, Ruben SM, Ni J, Feng P;
 XX WPI: 2002-281068/32.
 DR N-PSDB: AAD33281.
 XX
 PT Novel nucleic acid molecules comprising a polynucleotide encoding human
 PT tumor necrosis factor receptor (TNFR)-6alpha and 6beta polypeptides
 PT useful for treating disease e.g. inflammatory and autoimmune disorders
 PT
 XX
 PS Claim 1: Fig 1: 350pp; English.
 XX
 CC The invention relates to human tumour necrosis factor receptor (TNFR)-
 CC 6alpha and 6beta protein and their corresponding nucleic acids. The
 CC invention provides screening methods for identifying agonists and
 CC antagonists of TNFR-6alpha and 6beta activity. The invention also
 CC provides diagnostic and therapeutic methods for detecting and treating
 CC immune system-related disorders. The method is useful for treating or
 CC preventing an inflammatory disease or disorder selected from bowel
 CC disease, encephalitis, atherosclerosis and psoriasis, an autoimmune
 CC arthritis or disorder selected from systemic lupus erythematosus,
 CC rheumatoid arthritis, multiple sclerosis, Crohn's disease,
 CC and autoimmune encephalitis, graft versus host disease (GVHD), and an
 CC allergy or asthma. The present sequence is human TNFR-6alpha protein.
 CC
 XX
 SQ Sequence 300 AA;
 Query Match 100.0%; Score 1634; DB 23; Length 300;
 Best Local Similarity 100.0%; Pred. NO. 1.4e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 Oy 1 MRALEGPGLSLCLVIALPALLPVPAVGVAEPTTPYPRDAETGERLYCAACPPGTFVQR 60
 Db 1 MRALEGPGLSLCLVIALPALLPVPAVGVAEPTTPYPRDAETGERLYCAACPPGTFVQR 60
 Oy 61 PCRDSPTTCGCPRRHTQFWNTLERRCYCNVLGGEREEBARACHAHNACRCRTGFF 120
 Db 61 PCRDSPTTCGCPRRHTQFWNTLERRCYCNVLGGEREEBARACHAHNACRCRTGFF 120
 Oy 121 AHAGFCEHASCPRGAGVIAGTSPONTQCCPCPGTFSASSSSSECCOPHRNCATGLA 180
 Db 121 AHAGFCEHASCPRGAGVIAGTSPONTQCCPCPGTFSASSSSSECCOPHRNCATGLA 180
 Oy 181 LNVGSSSHDILCTSGTFPLSTRVPGAEECEERAVIDFVAFODISIKRLQLQALEAPE 240
 Db 181 LNVGSSSHDILCTSGTFPLSTRVPGAEECEERAVIDFVAFODISIKRLQLQALEAPE 240
 Oy 241 GMPPTPRAGRAALQKLRRLTELIGADGALLVRLLOALVYARMPGLERSVREFFLVH 300
 Db 241 GMPPTPRAGRAALQKLRRLTELIGADGALLVRLLOALVYARMPGLERSVREFFLVH 300
 RESULT 25
 AAG73740
 ID AAG73740 standard; Protein: 341 AA.
 AC AAG73740;
 XX
 DT 03-SEP-2001 (first entry)
 XX
 DE Human colon cancer antigen protein SEQ ID NO:4504.
 XX
 KW Human; colon cancer; colon cancer antigen; diagnosis; detection;
 XX colorectal carcinoma; chromosome 20.
 OS Homo sapiens.
 XX
 PN WO200122920-A2.
 XX
 PD 05-APR-2001.
 XX
 PF 28-SEP-2000; 2000WO-US26524.
 XX

PR 29-SEP-1999; 99US-0157137.
 PR 03-NOV-1999; 99US-0153280.
 XX
 PA (HUMA-) HUMAN GENOME SCI INC.
 XX
 PI Ruben SM, Barash SC, Birse CE, Rosen CA;
 XX WPI: 2001-235357/24.
 DR N-PSDB: AAH33171.
 XX
 PT Nucleic acids encoding 4277 human colon cancer-associated polypeptides,
 PT useful for preventing, diagnosing and/or treating colorectal cancers -
 PT
 XX
 PS Claim 11: Page 6304-6306; 9803pp; English.
 CC AAH32943 to AAH37195 and AAG73514 to AAG77788 represent human colon
 CC cancer-associated nucleic acid molecules (N) and proteins (P), where
 CC the proteins are collectively known as colon cancer antigens. The colon
 CC cancer antigens have cytostatic activity and can be used in gene
 CC therapy and vaccine production. N and P may be used in the prevention,
 CC diagnosis and treatment of diseases associated with inappropriate P
 CC expression. For example, N and P may be used to treat disorders
 CC associated with decreased expression by rectifying mutations or deletions
 CC in a patient's genome that affect the activity of P by expressing
 CC inactive proteins or to supplement the patients own production of P.
 CC Additionally, N may be used to produce the colon cancer-associated Ps,
 CC by inserting the nucleic acids into a host cell and culturing the cell
 CC to express the proteins. N and P can be used in the prevention, diagnosis
 CC and treatment of colorectal carcinomas and cancers. AAH37196 to AAH37204
 CC and AAH77789 represent sequences used in the exemplification of the
 CC present invention.
 CC N.B. Pages 666 to 682 and page 7053 of the sequence listing were
 CC missing at time of publication, meaning no sequences are present for
 CC SEQ ID NO:1027 to 1052, 7921 and 7922.
 XX
 SQ Sequence 341 AA;
 Query Match 100.0%; Score 1634; DB 22; Length 341;
 Best Local Similarity 100.0%; Pred. NO. 1.6e-121;
 Matches 300; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 Oy 1 MRALEGPGLSLCLVIALPALLPVPAVGVAEPTTPYPRDAETGERLYCAACPPGTFVQR 60
 Db 42 MRALEGPGLSLCLVIALPALLPVPAVGVAEPTTPYPRDAETGERLYCAACPPGTFVQR 101
 Oy 61 PCRDSPTTCGCPRRHTQFWNTLERRCYCNVLGGEREEBARACHAHNACRCRTGFF 120
 Db 61 PCRDSPTTCGCPRRHTQFWNTLERRCYCNVLGGEREEBARACHAHNACRCRTGFF 120
 Oy 102 PCRDSPTTCGCPRRHTQFWNTLERRCYCNVLGGEREEBARACHAHNACRCRTGFF 161
 Db 102 PCRDSPTTCGCPRRHTQFWNTLERRCYCNVLGGEREEBARACHAHNACRCRTGFF 161
 Oy 121 AHAGFCEHASCPRGAGVIAGTSPONTQCCPCPGTFSASSSSSECCOPHRNCATGLA 180
 Db 121 AHAGFCEHASCPRGAGVIAGTSPONTQCCPCPGTFSASSSSSECCOPHRNCATGLA 180
 Oy 162 AHAGFCEHASCPRGAGVIAGTSPONTQCCPCPGTFSASSSSSECCOPHRNCATGLA 221
 Db 162 AHAGFCEHASCPRGAGVIAGTSPONTQCCPCPGTFSASSSSSECCOPHRNCATGLA 221
 Oy 181 LNVGSSSHDILCTSGTFPLSTRVPGAEECEERAVIDFVAFODISIKRLQLQALEAPE 240
 Db 222 LNVGSSSHDILCTSGTFPLSTRVPGAEECEERAVIDFVAFODISIKRLQLQALEAPE 281
 Oy 241 GMPPTPRAGRAALQKLRRLTELIGADGALLVRLLOALVYARMPGLERSVREFFLVH 300
 Db 282 GMPPTPRAGRAALQKLRRLTELIGADGALLVRLLOALVYARMPGLERSVREFFLVH 341
 RESULT 26
 AAY77458
 ID AAY77458 standard; Protein: 300 AA.
 AC AAY77458;
 XX
 DT 05-JUN-2000 (first entry)
 XX
 DE Human TNF receptor-like protein, HDTEA84.
 XX
 KW TNF receptor family; tumour necrosis factor; HDTEA84; HSLJD37R;

KW Rank-like protein; RANKL; immune disorder; inflammation; allergy;
 KW immunosuppressant; antirheumatic; antirheumatoid; antinflammatory;
 KW dermatological; antithyroid.
 XX Homo sapiens.
 XX WO200001817-A2.
 XX 13-JAN-2000.
 PD 13-JAN-2000.
 XX 06-JUL-1999; 99WO-US12366.
 XX 06-JUL-1999; 98US-0110938.
 PR 06-JUL-1998; 98US-0110938.
 PR 13-JUL-1998; 98US-0114466.
 PR 23-JUL-1998; 98US-0093897.
 PR 12-AUG-1998; 98US-0132968.
 PR 18-AUG-1998; 98US-0136214.
 PR 11-SEP-1998; 98US-0099999.
 XX (SCHE) SCHERING CORP.
 PA Bates EEM, Lebecque SUE, Murphy EE, Mattson JD, Gorman DM;
 PI Hedrick JA, Wang L, Zlotnik A, Murgolo NJ, Greene JR, Johnston JA;
 PI Bazan JF, Mahony D, Lees EM.
 XX WPI: 2000-171015/15.
 DR N-PSDB: AAZ92404.
 XX New isolated mammalian genes, used to develop products for treating
 PT e.g. immune, inflammatory or allergic abnormalities, cancers or
 PT degenerative conditions -
 XX Claim 24: Page 157; 218pp; English.
 PS The invention relates to a number of primate and/or rodent proteins, and
 XX the genes which encode them. The invention encompasses human dendritic
 CC cell prostaglandin transporter (DC-PGT); the TNF (tumour necrosis
 CC factor) receptor family-related proteins HTR84, HSLJD37R and RANKL;
 CC human CC chemokine HCC5; human dendritic proteins Dnbl1 and Dnbl
 CC 12; human MD-1 and human and murine MD-2 proteins, which exhibit the
 CC properties of ligands for proteins comprising a leucine-rich motif
 CC (LRR); human cyclin E2; cDNAs encoding these proteins; and antibodies
 CC against these proteins. The proteins can be used for modulating the
 CC physiology or development of a cell. They can be used to mediate uptake
 CC of substrates (e.g., prostaglandin-like molecules), to modulate or
 CC mediate cellular interactions (e.g., induce or prevent trafficking,
 CC proliferation, or differentiation of cells), or are intracellular
 CC proteins which are important in various cellular processes such as the
 CC deubiquitination of proteins or cell cycle regulation. The products can
 CC be used for treating medical conditions such as immune, inflammatory or
 CC allergic disorders, or abnormal cellular proliferation, for example,
 CC cancers or degenerative conditions. They can be used to modulate immune
 CC responses in disease states e.g., autoimmune disorders, including
 CC rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's
 CC autoimmune thyroiditis, as well as acute and chronic inflammatory
 CC responses in which T cell activation, expansion, and/or immunological T
 CC cell memory play an important role. Sequences AAY77458-Y77461 and
 CC AAY77465-Y77468 represent TNF receptor family-related proteins. AAY77458
 CC is the human protein HTR84, AAY77459-Y77461 are human HSLJD37R
 CC proteins, AAY77465 is murine Rank-like protein RANKL, and AAY77466-Y77468
 CC are human RANKL proteins.
 CC
 XX Sequence 300 AA;
 XX
 XX Query Match 99.1%; Score 1620; DB 21; Length 300;
 XX Best Local Similarity 99.3%; Pred. No. 1.8e-120;
 XX Matches 296; Conservative 0; Mismatches 2; Indels 0; Gaps 0;
 OY 1 MRALEGGSLTCLVIALPALPAPVAVGAEPTPTYPMPADATGGERLVCAQCPGPFVOR 60
 DB 1 MRALEGGSLTCLVIALPALPAPVAVGAEPTPTYPMPADATGGERLVCAQCPGPFVOR 60
 OY 61 PCRBDSPPTGCPPRHYTFWMYLERCRYCNVLCGEREEBARACHATNHRACRCRTGTF 120

DB 61 PCRBDSPMTGCPPPRHYYTFWMYLERCRYCNVLCGEREEBARACHATNHRACRCRTGTF 120
 OY 121 AHAGFCLEHASCPGACVIAAGPSONTOGCPGPFSSASSSSSECCOHRNCTALGTA 180
 DB 121 AHAGFCLEHASCPGACVIAAGPSONTOGCPGPFSSASSSSSECCOHRNCTALGTA 180
 OY 181 LNVPGSSHDITCTGTFPLSTFVPGAECECAVDFVAFODISIKRLQRLQALEAPE 240
 DB 181 LNVPGSSHDITCTGTFPLSTFVPGAECECAVDFVAFODISIKRLQRLQALEAPE 240
 OY 241 GWGPTPRAGRAALQKRRRLTELLGAQDALLVRLQALVARMPGLERSVBRFLPVH 300
 DB 241 GWGPTPRAGRAALQKRRRLTELLGAQDALLVRLQALVARMPGLERSVBRFLPVH 300
 RESULT 27
 AAB19710
 ID AAB19710 standard; Protein: 300 AA.
 XX
 AC AAB19710;
 XX
 DT 05-FEB-2001 (first entry)
 XX
 DE Human FAS ligand inhibitor protein FLINT native sequence.
 XX
 KW FLINT: FAS ligand inhibitor protein; human; protease resistant;
 KW acute lung injury; acute respiratory distress syndrome;
 KW chronic obstructive pulmonary disease; pulmonary fibrosis;
 KW ulcerative colitis; therapy; organ transplantation.
 XX
 OS Homo sapiens.
 XX
 FH Key Location/Qualifiers
 FT Peptide 1..29
 FT Protein /label= Signal_peptide
 FT /label= Mature_protease
 FT Cleavage-site 247..248
 FT /note= "cleaved by trypsin-like proteases"
 XX
 PN WO200058466-A2.
 XX
 PD 05-OCT-2000.
 XX
 PF 20-MAR-2000; 2000WO-US06418.
 XX
 PR 30-MAR-1999; 99US-0126839.
 PR 21-JUN-1999; 99US-0140073.
 PR 04-AUG-1999; 99US-0147071.
 PR 20-OCT-1999; 99US-0160524.
 PR 21-OCT-1999; 99US-0160669.
 PR 20-DEC-1999; 99US-0172274.
 PR 26-JAN-2000; 2000US-0178184.
 XX
 XX (ELI) LILLY & CO ELI.
 XX
 XX Micranovic R, Rathnachalam R, Witche DR;
 DR WPI: 2000-664925/64.
 DR N-PSDB: AAA88731.
 XX
 XX Novel protease resistant FAS ligand inhibitor protein analogues
 PT resistant to in vivo or in vitro proteolysis at amino acid position 218
 PT of the mature protein, useful for treating autoimmune diseases -
 XX
 XX Disclosure: Page 97-98; 100pp; English.
 XX
 XX The present sequence is that of human FAS ligand inhibitor protein
 CC FLINT native protein. FLINT is a tumour necrosis factor receptor
 CC homologue that binds FAS ligand, preventing its interaction with
 CC FAS. This interaction is implicated in runaway apoptosis and
 CC inflammatory disease. FLINT also binds to LIGHT, a membrane-bound

CC ligand, which may play a role in immune modulation and apoptosis.
 CC The invention relates to novel FLINT analogues (see also AAB19706-09)
 CC that are resistant to proteolysis by trypsin-like proteases between
 CC positions 218 and 219 of the FLINT mature protein sequence (see
 CC AAB19705), equivalent to positions 247 and 248 of the present
 CC sequence. The analogues have amino acid substitutions in the
 CC region comprising amino acids 214-222, and optionally at residues
 CC 34, 36, 132, 194 and/or 196, of the mature protein. Nucleic acids,
 CC vectors and transformed host cells for recombinant production of
 CC the analogues are claimed. FLINT cDNA (see AAB88731) is used as a
 CC template for introducing the required point mutations. The
 CC protease resistant FLINT analogues are used to prevent or treat
 CC acute lung injury, acute respiratory stress syndrome, ulcerative
 CC colitis, chronic obstructive pulmonary disease, pulmonary
 CC fibrosis, to inhibit T lymphocyte activation, and to facilitate
 CC organ preservation for transplantation (claimed).

XX Sequence 300 AA:

Query Match 99.1%; Score 1619; DB 21; Length 300;

Best Local Similarity 99.3%; Pred. No. 2.2e-120;
 Matches 298; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

QY 1 MRALEGGSLICLVLPALLPVPVAVGVAETPTYPWRDAETGERLYCAOCPPTFYQR 60
 DB 1 MRALEGGSLICLVLPALLPVPVAVGVAETPTYPWRDAETGERLYCAOCPPTFYQR 60
 QY 61 PCRRDPTTCGCPRRHNTQFNNYLERCRVCNVLCGEREEERACHATHNRACRCRTGEF 120
 DB 61 PCRRDPTTCGCPRRHNTQFNNYLERCRVCNVLCGEREEERACHATHNRACRCRTGEF 120
 QY 121 AHAGFCLEHASCPCGAGVIAPGTPSQNTQCPGPTFSASSSSSECCOPHNCTALGIA 180
 DB 121 AHAGFCLEHASCPCGAGVIAPGTPSQNTQCPGPTFSASSSSSECCOPHNCTALGIA 180
 QY 121 LNVPGSSSHDPLCTSGTGPPLSTRVPGABECERAVIDVAFODISIKRLQRLQALEAPE 240
 DB 181 LNVPGSSSHDPLCTSGTGPPLSTRVPGABECERAVIDVAFODISIKRLQRLQALEAPE 240
 DB 181 LIVPGSSSHDPLCTSGTGPPLSTRVPGABECERAVIDVAFODISIKRLQRLQALEAPE 240
 QY 241 GMAPPPRAGRAALQKLRRLTELIGADGALVLLQALRVARRMPGLERSVREFFLPVH 300
 DB 241 GMAPPPRAGRAALQKLRRLTELIGADGALVLLQALRVARRMPGLERSVREFFLPVH 300

RESULT 28
 AAY96597

ID AAY96597 standard; Protein; 300 AA.

XX AAY96597;

DT 26-SEP-2000 (first entry)

XX Human FLINT.

DE Human FLINT.

XX FLINT; osteoprotegerin 3, OPG3; tumour necrosis factor receptor; TNFR;

KW FasL; LIGHT; apoptosis; pro-inflammatory; hepatotropic; vasotropic;

KW anti-diabetic; anti-anemic; neuroprotective; anti-ulcer; cytostatic;

KW anti-inflammatory; antibacterial; immunosuppressive.

XX Homo sapiens.

OS Homo sapiens.

XX Key

XX Peptide

XX Protein

XX WO200037094-A2.

XX 29-JUN-2000.

XX 21-DEC-1999; 99WO-US30734.

PR 22-DEC-1998; 98US-0113407.
 PR 30-MAR-1999; 99WO-US06797.
 PR 20-OCT-1999; 99US-0172239.
 XX (ELIL) LILLY & CO ELI.
 PA Cohen FJ, Posada JA, Wierda D;
 XX WPI: 2000-475441/41.
 DR N-PSDB: AAA51076.

XX Use of mature FLINT for treating e.g. acute respiratory distress
 PR syndrome, ulcerative colitis or ischemic injury during organ
 PT transplantation
 PS Example 1; Fig 2A-B; 125pp; English.

CC Human FLINT (also known as osteoprotegerin 3) is a new tumour necrosis
 CC factor receptor (TNFR) superfamily member, which binds FasL and LIGHT and
 CC prevents FasL-Fas interaction. Mature FLINT (mFLINT) inhibits FasL-Fas
 CC mediated apoptotic and pro-inflammatory activity. mFLINT is useful for
 CC treating acute respiratory distress syndrome, treating or inhibiting
 CC ulcerative colitis, inhibiting ischemic injury during organ
 CC transplantation or for organ preservation during transplantation. mFLINT
 CC can also be used to treat acute liver failure, inflammation of the liver,
 CC abnormal (hepatocyte) apoptosis, sepsis, disorders associated with
 CC inflammation, hepatitis, ischemia, hypercoagulation or reperfusion,
 CC damage to a cardiac myocyte resulting from abnormal myocardial ischemia,
 CC Type I diabetes, cancer, damage to an innocent bystander tissue induced
 CC by a chemotherapeutic or therapeutic irradiation, aplastic anaemias,
 CC myelodysplastic syndromes and pancytopenic conditions.

XX Sequence 300 AA:

Query Match 99.1%; Score 1619; DB 21; Length 300;

Best Local Similarity 99.3%; Pred. No. 2.2e-120;
 Matches 298; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

QY 1 MRALEGGSLICLVLPALLPVPVAVGVAETPTYPWRDAETGERLYCAOCPPTFYQR 60
 DB 1 MRALEGGSLICLVLPALLPVPVAVGVAETPTYPWRDAETGERLYCAOCPPTFYQR 60
 QY 61 PCRRDPTTCGCPRRHNTQFNNYLERCRVCNVLCGEREEERACHATHNRACRCRTGEF 120
 DB 61 PCRRDPTTCGCPRRHNTQFNNYLERCRVCNVLCGEREEERACHATHNRACRCRTGEF 120
 QY 121 AHAGFCLEHASCPCGAGVIAPGTPSQNTQCPGPTFSASSSSSECCOPHNCTALGIA 180
 DB 121 AHAGFCLEHASCPCGAGVIAPGTPSQNTQCPGPTFSASSSSSECCOPHNCTALGIA 180
 QY 121 LNVPGSSSHDPLCTSGTGPPLSTRVPGABECERAVIDVAFODISIKRLQRLQALEAPE 240
 DB 181 LNVPGSSSHDPLCTSGTGPPLSTRVPGABECERAVIDVAFODISIKRLQRLQALEAPE 240
 DB 181 LIVPGSSSHDPLCTSGTGPPLSTRVPGABECERAVIDVAFODISIKRLQRLQALEAPE 240
 QY 241 GMAPPPRAGRAALQKLRRLTELIGADGALVLLQALRVARRMPGLERSVREFFLPVH 300
 DB 241 GMAPPPRAGRAALQKLRRLTELIGADGALVLLQALRVARRMPGLERSVREFFLPVH 300

RESULT 29
 AAE03570

ID AAE03570 standard; Protein; 300 AA.

XX AAE03570;

DT 04-AUG-2001 (first entry)

XX Human fas ligand inhibitory protein (FLINT).

DE Human fas ligand inhibitory protein (FLINT).

XX Human fas ligand inhibitory protein; FLINT; acute lung injury; ALI;

KW TNFR; tumour necrosis factor receptor; ulcerative colitis; ARDS;

KW acute respiratory distress syndrome; pulmonary fibrosis; PF; therapy;

KW chronic obstructive pulmonary disease; COPD; acute lung injury; goitre;

| | |
|----|--|
| KW | rhematoid arthritis; fibroproliferative lung disease; ischaemia; sepsis; |
| KW | fibrotic lung disease; human immunodeficiency virus; HIV; osteoporosis; |
| KW | chronic renal failure; graft-vs-host disease; cutaneous inflammation; |
| KW | vascular leak syndrome; Helicobacter pylori infection; atherosclerosis; |
| KW | insulin dependent diabetes mellitus (IDDM); inflammatory bowel disease; |
| KW | Crohn's disease; pancreatitis; cancer; autoimmune disease; psoriasis; |
| KW | Down's syndrome; multiple sclerosis; cytostatic; nootropic; |
| KW | neuroprotective; vasotropic. |
| OS | |
| XX | Homo sapiens. |
| PN | WO200142463-A1. |
| XX | |
| PD | 14-JUN-2001. |
| XX | |
| PE | 29-NOV-2000; 2000MO-US30166. |
| PR | 07-DEC-1999; 99US-0169367. |
| PR | 07-DEC-1999; 99US-0169381. |
| PR | 07-DEC-1999; 99US-0169412. |
| PR | 23-MAR-2000; 2000US-0191430. |
| XX | |
| XX | (ELIL) LILLY & CO ELI. |
| PA | |
| PI | Lu J, Witcher DR; |
| DR | WPI: 2001-381684/40. |
| DR | N-PSDB: AAD07385. |
| XX | |
| PT | New FLINT polypeptide for treating and/or preventing acute lung injury, |
| PT | acute respiratory distress syndrome, ulcerative colitis, and |
| PT | graft-versus-host disease, comprises O-linked or N-linked |
| PT | oligosaccharides - |
| XX | |
| PS | Disclosure: Page 56-57; 60pp; English. |
| XX | |
| CC | The present sequence is human fas ligand inhibitory protein |
| CC | (FLINT). FLINT, a homologue of tumour necrosis factor receptor |
| CC | protein (TNFR), binds fas ligand (FasL) and thereby preventing the |
| CC | interaction of FasL with fas. FLINT comprising O-linked or N-linked |
| CC | oligosaccharides is useful for preventing or treating acute lung injury |
| CC | (ALI), acute respiratory distress syndrome (ARDS), ulcerative colitis, |
| CC | chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis (PF), |
| CC | to facilitate organ preservation for transplantation and to inhibit T |
| CC | lymphocyte activation. FLINT is useful for treating and/or preventing |
| CC | diseases such as Rheumatoid arthritis, fibroproliferative lung disease, |
| CC | fibrotic lung disease, acute lung injury, human immunodeficiency virus |
| CC | (HIV), ischaemia, brain trauma/injury, chronic renal failure, graft-vs- |
| CC | host disease, cutaneous inflammation, vascular leak syndrome, |
| CC | Helicobacter pylori infection, gotitre, atherosclerosis, insulin dependent |
| CC | diabetes mellitus (IDDM), osteoporosis, inflammatory bowel disease, |
| CC | Crohn's disease, sepsis, pancreatitis, cancer, autoimmune disease such as |
| CC | psoriasis, Down's syndrome, and multiple sclerosis. |
| CC | |
| XX | |
| SQ | Sequence 300 AA: |
| | |
| | Query Match 99.1%; Score 1619; DB 22; Length 300; |
| | Best Local Similarity 99.3%; Pred. No. 2, 2e-120; |
| | Matches 298; Conservative 0; Mismatches 2; Indels 0; Gaps 0 |
| OY | 1 MRALEGPILSLCLVIALPALLPVAIVGVAVPTPTYPWMDATGERTVCAQCPRGFVOR 60 |
| Db | 1 MRALEGPILSLCLVIALPALLPVAIVGVAVPTPTYPWMDATGERTVCAQCPRGFVOR 60 |
| OY | 61 PCRDRSPTTCGCPPRHYTQFWNYLERCYCNVLGGEREEARACHATHNRACRCRTGFF 120 |
| Db | 61 PCRDRSPTTCGCPPRHYTQFWNYLERCYCNVLGGEREEARACHATHNRACRCRTGFF 120 |
| OY | 121 AHAGCIEHASOPPAGVIAPEPTPSONTOCPCPGTSSASSSSSSOCPHNNCTALGIA 180 |
| Db | 121 AHAGCIEHASOPPAGVIAPEPTPSONTOCPCPGTSSASSSSSSOCPHNNCTALGIA 180 |
| OY | 181 LNVGSSSHDTLCTCTGTFPLSTRVGAEECEERAVIDFAFDISIKRLQRLQALAEPE 240 |

[illegible]

Db 1 MRALEGGSLCLCLVIALPALLPVPAVGVAEPTPTVPMRDAETGERLVCAQCPCPGTFVOR 60
 QY 61 PCRRDSEPTTCGCPRRHYTOFMWYLERCRVCNVLCEGEEAEACATNHRACRCRTGFF 120
 Db 61 PCRRDSEPTTCGCPRRHYTOFMWYLERCRVCNVLCEGEEAEACATNHRACRCRTGFF 120
 QY 121 AAAGFCLAEHASCPCPGAGVIAPGTPSONTOCCPCPGTFSSASSSSSECCQPHRNCATLGIA 180
 Db 121 AAAGFCLAEHASCPCPGAGVIAPGTPSONTOCCPCPGTFSSASSSSSECCQPHRNCATLGIA 180
 QY 181 LNVPGSSSHDTLCTSCGTFPLSTRVPAGEECERAVIDFAFODISIKRLQRLQALEAPE 240
 Db 181 LNVPGSSSHDTLCTSCGTFPLSTRVPAGEECERAVIDFAFODISIKRLQRLQALEAPE 240
 QY 241 GMGPTPRAGRAALQKLRRRLTELLGAODGALLVRLQALRVARMGLESVERERFLPVH 300
 Db 241 GMGPTPRAGRAALQKLRRRLTELLGAODGALLVRLQALRVARMGLESVERERFLPVH 300
 RESULT 33
 ID AAE14580 standard; Protein: 300 AA.
 AC AAE14580;
 DT 01-JUL-2002 (first entry)
 DE Human FLINT analog.
 DE Human FLINT analog.
 KM FLINT; FAS ligand inhibitory protein; pulmonary; lung; apoptosis;
 KM organ failure; liver; pancreas; inflammatory disease;
 KM neutrophil; sepsis; acute respiratory distress syndrome;
 KM acute lung injury; systemic inflammatory response syndrome; SIRS;
 KM multiple organ dysfunction; MODS; human.
 OS Homo sapiens.
 PN MO200209668-A2.
 PD 07-FEB-2002.
 PF 20-JUL-2001; 2001MO-US21105.
 PR 02-AUG-2000; 2000US-222476P.
 PA (ELIL) LILLY & CO ELI.
 PI Micranovic R, Wilcher DR;
 DR WPI; 2002-206149/26.
 DR N-PSDB; AAD27869.
 XX Administering FLINT (FAS ligand inhibitory protein) or FLINT analog,
 PT useful for treating e.g. sepsis or respiratory distress syndrome,
 PT involves pulmonary administration of a therapeutic amount of the FLINT
 PT or FLINT analog -
 XX Disclosure: Page 34-35; 35pp; English.
 XX The invention relates to a new method of administering FLINT
 CC (FAS ligand inhibitory protein) or FLINT analog that involves pulmonary
 CC administration of a therapeutic amount of FLINT through lungs and
 CC significantly reduces or eliminates the need for administering FLINT by
 CC injection or other routes of administration. The method is useful in
 CC treating disorders related to enhanced apoptosis (e.g. organ failure
 CC in liver, kidneys and pancreas) and inflammatory diseases associated with
 CC neutrophil activation (e.g. sepsis, acute respiratory distress syndrome,
 CC acute lung injury, systemic inflammatory response syndrome (SIRS) and
 CC multiple organ dysfunction (MODS)). The method minimises the pain
 CC and discomfort of injection methods. The present sequence is human
 CC FLINT analog.
 XX

SQ Sequence 300 AA;
 Query Match 99.1%; Score 1619; DB 23; Length 300;
 Best Local Similarity 99.3%; Pred. No. 2, 2e-120;
 Matches 298; Conservative 0; Mismatches 2; Indels 0; Gaps 0;
 QY 1 MRALEGGSLCLCLVIALPALLPVPAVGVAEPTPTVPMRDAETGERLVCAQCPCPGTFVOR 60
 Db 1 MRALEGGSLCLCLVIALPALLPVPAVGVAEPTPTVPMRDAETGERLVCAQCPCPGTFVOR 60
 QY 61 PCRRDSEPTTCGCPRRHYTOFMWYLERCRVCNVLCEGEEAEACATNHRACRCRTGFF 120
 Db 61 PCRRDSEPTTCGCPRRHYTOFMWYLERCRVCNVLCEGEEAEACATNHRACRCRTGFF 120
 QY 121 AAAGFCLAEHASCPCPGAGVIAPGTPSONTOCCPCPGTFSSASSSSSECCQPHRNCATLGIA 180
 Db 121 AAAGFCLAEHASCPCPGAGVIAPGTPSONTOCCPCPGTFSSASSSSSECCQPHRNCATLGIA 180
 QY 181 LNVPGSSSHDTLCTSCGTFPLSTRVPAGEECERAVIDFAFODISIKRLQRLQALEAPE 240
 Db 181 LNVPGSSSHDTLCTSCGTFPLSTRVPAGEECERAVIDFAFODISIKRLQRLQALEAPE 240
 QY 241 GMGPTPRAGRAALQKLRRRLTELLGAODGALLVRLQALRVARMGLESVERERFLPVH 300
 Db 241 GMGPTPRAGRAALQKLRRRLTELLGAODGALLVRLQALRVARMGLESVERERFLPVH 300
 RESULT 34
 ID AAY42183 standard; Protein: 302 AA.
 AC AAY42183;
 DT 17-DEC-1999 (first entry)
 DE Human FLINT #2 protein sequence.
 DE Human FLINT #2 protein sequence.
 KM Human; FLINT; mFLINT; OPG3; tumour necrosis factor receptor; FasL;
 KM apoptosis; inflammation; cancer; diabetes; acute liver failure;
 KM sepsis; hepatitis; ischaemia-associated injury; hypercoagulation;
 KM reperfusion-associated injury; aplastic anaemia; differentiation;
 KM growth; myelodysplastic syndrome; pancytopenic condition;
 KM myocardial ischaemia.
 OS Homo sapiens.
 PN WO950413-A2.
 PD 07-OCT-1999.
 PF 30-MAR-1999; 99MO-US06797.
 PR 30-MAR-1998; 98US-0079856.
 PR 20-MAY-1998; 98US-0086074.
 PR 09-SEP-1998; 98US-009643.
 PR 17-DEC-1998; 98US-0112577.
 PR 18-DEC-1998; 98US-0112703.
 PR 18-DEC-1998; 98US-0112933.
 PR 22-DEC-1998; 98US-0113407.
 PA (ELIL) LILLY & CO ELI.
 PI Bunoil TF, Dou S, Glasebrook AL, Gould KE, Hale JE, Heuer JG;
 PI Hui KY, Kharitonov A, Mizrihi J, Na S, Noblitt TW, Reidy CA;
 PI Song HY, Wang J, Wu X, Zuckerman SH;
 DR WPI; 1999-591319/50.
 DR N-PSDB; AA225376.
 XX use of mature FLINT for treating acute liver failure, inflammation,
 PT cancer, and diabetes - by prevention of FasL-Fas mediated apoptotic
 PT and proinflammatory activity
 XX

PS Example 2; Fig 2; 99pp; English.

XX
 CC The present invention describes therapeutic applications of mature FLINT
 CC (mFLINT) for use in the treatment of acute liver failure. Mature FLINT
 CC (mFLINT), which is a member of the tumour necrosis factor receptor
 CC superfamily, is used for treating acute liver failure, inflammation of
 CC the liver, abnormal hepatocyte apoptosis, sepsis, a disorder associated
 CC with inflammation, hepatitis, abnormal apoptosis, an ischaemia-associated
 CC injury or disorder such as hypercoagulation (including use with
 CC thrombolytic or anti-thrombolytic agents), reperfusion-associated injury
 CC or disorder, type I diabetes, cancer, cell damage or damage to an
 CC innocent bystander tissue that is induced by a chemotherapeutic agent or
 CC therapeutic irradiation, treating haematopoietic progenitor cells that
 CC have been exposed to therapeutic radiation or chemotherapy, aplastic
 CC anaemia, myelodysplastic syndrome or a pancytopenic condition. mFLINT is
 CC also used for promoting the growth or differentiation of a haematopoietic
 CC progenitor cell or CD34+ cell and preventing damage to a cardiac myocyte
 CC resulting from abnormal myocardial ischaemia. The present sequence
 CC represents human FLINT.

XX
 SQ Sequence 302 AA;

Query Match 98.5%; Score 1610; DB 20; Length 302;
 Best Local Similarity 98.7%; Pred. No. 1.1e-119;
 Matches 298; Conservative 0; Mismatches 2; Indels 2; Gaps 1;

QY 1 MRALBPGSLSLCTLVLPALPVPVAVGVAETPTVPMWDAETGERLVCAQCPRGTFVOR 60
 1 MRALBPGSLSLCTLVLPALPVPVAVGVAETPTVPMWDAETGERLVCAQCPRGTFVOR 60
 DB 61 PCRDSPTTCGPPRPHHYQFMWYLERCRVCNVLCGEREERARACHATNHRACRCRTG 120
 61 PCRDSPTTCGPPRPHHYQFMWYLERCRVCNVLCGEREERARACHATNHRACRCRTG 120
 QY 119 FRAHGFLEHASCPRGAGVIAAPGTSONTOCOPCPPTFSASSSSQCPHNRCTALG 178
 119 FRAHGFLEHASCPRGAGVIAAPGTSONTOCOPCPPTFSASSSSQCPHNRCTALG 178
 DB 121 FRAHGFLEHASCPRGAGVIAAPGTSONTOCOPCPPTFSASSSSQCPHNRCTALG 180
 121 FRAHGFLEHASCPRGAGVIAAPGTSONTOCOPCPPTFSASSSSQCPHNRCTALG 180
 QY 179 LALNVGSSSHDTLCTSCGTGFPPLSTRVPGAEECEERAVIDVFAODISIKRLQRLALE 238
 179 LALNVGSSSHDTLCTSCGTGFPPLSTRVPGAEECEERAVIDVFAODISIKRLQRLALE 238
 DB 181 LALNVGSSSHDTLCTSCGTGFPPLSTRVPGAEECEERAVIDVFAODISIKRLQRLALE 240
 181 LALNVGSSSHDTLCTSCGTGFPPLSTRVPGAEECEERAVIDVFAODISIKRLQRLALE 240
 QY 239 PEGWGPTRAGRAALQKLRRRLTELLGAODGALLVRLQALVAVAMPGLERSVRERFLP 298
 239 PEGWGPTRAGRAALQKLRRRLTELLGAODGALLVRLQALVAVAMPGLERSVRERFLP 298
 DB 241 PEGWGPTRAGRAALQKLRRRLTELLGAODGALLVRLQALVAVAMPGLERSVRERFLP 300
 241 PEGWGPTRAGRAALQKLRRRLTELLGAODGALLVRLQALVAVAMPGLERSVRERFLP 300
 QY 299 VH 300
 299 VH 300
 DB 301 WH 302
 301 WH 302

RESULT 35
 ABB41980
 ID ABB41980 standard; Protein; 326 AA.

XX
 AC ABB41980;
 XX
 DT 22-AUG-2002 (first entry)
 XX

DE Human ovarian antigen HTPCH84, SEQ ID NO:3112.

XX
 XX Human; ovarian antigen; ovary; ovarian; breast; cancer; tumour;
 KW Human cancer; breast cancer; tumour; reproductive system disorder;
 KW infertility; pregnancy disorder; anovulation; polycystic ovary syndrome;
 KW PCOS; ovarian cyst; dysmenorrhoea; endocrine disorder; infection;
 KW inflammatory condition; immune disorder; blood disorder;
 KW cardiovascular disorder; respiratory disorder; neurological disorder;
 KW gastrointestinal disorder; urinary system disorder; drug screening;
 KW gene therapy; chromosome mapping; forensic analysis;
 KW antibody preparation; cytostatic; immunomodulatory; neuroprotective;
 KW antiinflammatory; gynaecological; reproductive.

OS Homo sapiens.

XX
 PN WO200200677-A1.
 XX
 PD 03-JAN-2002.
 XX
 PF 07-JUN-2001; 2001WO-US18569.
 XX
 PR 07-JUN-2000; 2000US-209467P.
 XX
 PA (HUMA-) HUMAN GENOME SCI INC.
 XX
 PI Birse CE, Rosen CA;
 XX
 DR WPI: 2002-147878/19.
 XX
 DR N-PDSB; ABO55057.
 XX
 PT Isolated nucleic acid molecules encoding novel ovarian polypeptides,
 PT useful in the prevention, treatment and diagnosis of cancer (e.g.
 PT ovarian cancer), immune disorders, cardiovascular disorders and
 PT neurological diseases -

PS Claim 11: SEQ ID NO 3112; 2922pp; English.

XX
 CC The invention relates to 2175 novel human ovarian antigens (ABB41054-
 CC ABB43228) and to cDNAs encoding them (ABO54131-ABO56305), and also
 CC encompasses polypeptides 90% identical and polynucleotides 95% identical
 CC to the sequences of the invention. The invention additionally relates to
 CC recombinant vectors and host cells comprising human ovarian antigen
 CC polynucleotides, antibodies against human ovarian antigens, and the use
 CC of ovarian antigen polynucleotides and polypeptides in diagnosing,
 CC treating, prognosing or preventing various ovary and/or breast-related
 CC disorders. Such conditions include ovarian cancer and breast cancer, and
 CC metastatic tumours of ovarian or breast origin, reproductive system
 CC disorders (e.g., infertility, disorders of pregnancy, anovulation,
 CC polycystic ovary syndrome, ovarian cysts, and dysmenorrhoea), endocrine
 CC disorders, infections (e.g., chlamydia, HIV, toxoplasmosis, and toxic
 CC shock syndrome), inflammatory conditions (e.g., mastitis, oophoritis and
 CC vaginitis), immune disorders (e.g., congenital and acquired
 CC immunodeficiencies, autoimmune oophoritis, systemic lupus erythematosus),
 CC blood-related disorders (e.g., anaemia), cardiovascular disorders,
 CC respiratory disorders, neurological disorders, gastrointestinal disorders
 CC and urinary system disorders. Ovarian antigen polypeptides and
 CC polynucleotides may also be used in screening for compounds which
 CC modulate ovarian antigen expression or activity. The polynucleotides may
 CC further be used for gene therapy, chromosome mapping, in the
 CC identification of individuals and in forensic analysis, and the
 CC polypeptides may be used as food additives or to prepare antibodies
 CC useful in disease diagnosis, drug targeting and phenotyping. The present
 CC sequence represents a human ovarian antigen of the invention.
 CC Note: The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX
 SQ Sequence 326 AA;

Query Match 93.8%; Score 1532; DB 23; Length 326;
 Best Local Similarity 99.6%; Pred. No. 1.8e-113;
 Matches 280; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 MRALBPGSLSLCTLVLPALPVPVAVGVAETPTVPMWDAETGERLVCAQCPRGTFVOR 60
 1 MRALBPGSLSLCTLVLPALPVPVAVGVAETPTVPMWDAETGERLVCAQCPRGTFVOR 60
 DB 35 MRALBPGSLSLCTLVLPALPVPVAVGVAETPTVPMWDAETGERLVCAQCPRGTFVOR 94
 35 MRALBPGSLSLCTLVLPALPVPVAVGVAETPTVPMWDAETGERLVCAQCPRGTFVOR 94
 QY 61 PCRDSPTTCGPPRPHHYQFMWYLERCRVCNVLCGEREERARACHATNHRACRCRTG 120
 61 PCRDSPTTCGPPRPHHYQFMWYLERCRVCNVLCGEREERARACHATNHRACRCRTG 120
 DB 95 PCRDSPTTCGPPRPHHYQFMWYLERCRVCNVLCGEREERARACHATNHRACRCRTG 154
 95 PCRDSPTTCGPPRPHHYQFMWYLERCRVCNVLCGEREERARACHATNHRACRCRTG 154
 QY 121 AHAHGFLEHASCPRGAGVIAAPGTSONTOCOPCPPTFSASSSSQCPHNRCTALG 180
 121 AHAHGFLEHASCPRGAGVIAAPGTSONTOCOPCPPTFSASSSSQCPHNRCTALG 180
 DB 155 AHAHGFLEHASCPRGAGVIAAPGTSONTOCOPCPPTFSASSSSQCPHNRCTALG 214
 155 AHAHGFLEHASCPRGAGVIAAPGTSONTOCOPCPPTFSASSSSQCPHNRCTALG 214
 QY 181 LNVGSSSHDTLCTSCGTGFPPLSTRVPGAEECEERAVIDVFAODISIKRLQRLALE 240
 181 LNVGSSSHDTLCTSCGTGFPPLSTRVPGAEECEERAVIDVFAODISIKRLQRLALE 240

Db 215 LNVPGSSHPTLTSCGFIPLSTVRPGAECEGNAVIDEVAFODISIKRLQRLQALAEPE 274

QY 241 GWGPTPRAGRAALQKLRRRLTELLGAODGALLVRLQALR 281
 275 GWGPTPRAGRAALQKLRRRLTELLGAODGALLVRLQALR 315

Db 275 GWGPTPRAGRAALQKLRRRLTELLGAODGALLVRLQALR 315

RESULT 36

AAB03623
 ID AAB03623 standard; Protein: 300 AA.
 AC AAB03623;
 XX
 DT 03-JAN-2001 (first entry)
 DE Human Fas ligand inhibitor FLINT mutant.
 XX
 KW Human: Fas ligand inhibitor; FLINT; apoptosis; autoimmune disease;
 KW inflammation; infectious disease; ischaemia; Alzheimer's disease;
 KW Parkinson's disease; Crohn's disease; transplantation; mutant; mutein.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 FH Key
 FT Peptide
 FT Domain
 FT Misc-difference 10
 FT Misc-difference 16
 FT Misc-difference 23
 FT Misc-difference 27
 FT Misc-difference 30
 FT Misc-difference 31
 FT Misc-difference 33
 FT Misc-difference 41
 FT Misc-difference 42
 FT Domain
 FT Misc-difference 46
 FT Misc-difference 60
 FT Domain
 FT Misc-difference 86..122
 FT Misc-difference 104
 FT Domain
 FT Misc-difference 123..165
 FT Misc-difference 131
 FT Misc-difference 136
 FT Misc-difference 139
 FT Misc-difference 191
 FT Misc-difference 198
 FT Misc-difference 208
 FT Misc-difference 212
 FT Misc-difference

Location/Qualifiers
 1..29
 /label= signal_peptide
 1..42
 /label= domain_1
 /note= "wild-type Ser substituted by Leu"
 /note= "wild-type Leu substituted by Trp"
 /note= "wild-type Pro substituted by Leu"
 /note= "wild-type Val is substituted by Met"
 /note= "wild-type Val substituted by Ala"
 /note= "wild-type Ala substituted by Thr"
 /note= "wild-type Thr substituted by Ala"
 /note= "wild-type Ala substituted by Thr"
 /note= "wild-type Glu substituted by Asp"
 /label= domain_2
 /note= "wild-type Arg substituted by Trp"
 /note= "wild-type Arg substituted by Gln"
 /label= domain_3
 /note= "wild-type Ala substituted by Pro"
 /label= domain_4
 /note= "wild-type Ser substituted by Leu"
 /note= "wild-type Ala substituted by Thr"
 /note= "wild-type Ile substituted by Met"
 /note= "wild-type Thr substituted by Ala"
 /note= "wild-type Gly substituted by Ala"
 /note= "wild-type Ala substituted by Ala"
 /note= "wild-type Ala substituted by Thr"
 /note= "wild-type Glu substituted by Lys"

FT Misc-difference 238
 FT /note= "wild-type Ala substituted by Thr"
 FT Misc-difference 254
 FT /note= "wild-type Gln substituted by Arg"
 FT Misc-difference 258
 FT /note= "wild-type Arg substituted by Gln"
 FT Misc-difference 259
 FT /note= "wild-type Arg substituted by Gln"
 FT Misc-difference 266
 FT /note= "wild-type Gly substituted by Glu"
 FT Misc-difference 299
 FT /note= "wild-type Val substituted by Gly"
 XX
 PN W0200034782-A1.
 PD 15-JUN-2000.
 XX
 PF 07-DEC-1999; 99WO-US28696.
 XX
 PR 09-DEC-1998; 98US-0111575.
 PR 09-DEC-1998; 98US-0111580.
 PR 07-JAN-1999; 99US-0115069.
 XX
 PA (ELIL) LILLY & CO ELI.
 XX
 PI Rosteck PRJ, Song HY, Su EW;
 XX
 DR WPI: 2000-431379/37.
 XX
 PT Novel monkey Fas ligand inhibitor polypeptides, useful for treating
 PT inflammatory or autoimmune disease such as rheumatoid arthritis,
 PT infectious diseases such as chronic hepatitis, and
 PT ischaemia/Re-perfusion conditions -
 XX
 PS Claim 19; Page -; 101pp; English.
 XX
 CC The present sequence is a mutant protein sequence of the human Fas
 CC ligand inhibitor (FLINT). The FLINT protein is involved in cell-specific
 CC apoptosis, and can be used to treat inflammatory and autoimmune diseases
 CC such as rheumatoid arthritis, inflammatory bowel disease,
 CC graft-versus-host disease, diabetes, psoriasis and Graves' disease,
 CC infectious diseases such as HIV-induced lymphopenia, fulminant viral
 CC hepatitis B/C, chronic hepatitis and cirrhosis, and H. pylori-associated
 CC ulceration, ischaemia and reperfusion conditions including acute
 CC myocardial infarction, acute coronary syndrome, congestive heart failure
 CC and atherosclerosis, and Alzheimer's and Parkinson's diseases, acute
 CC lung injury and acute respiratory distress syndrome, Crohn's disease,
 CC brain trauma and injury, chronic glomerulonephritis, osteoporosis,
 CC aplastic anaemia, myelodysplasia, ulcerative colitis, Down's syndrome,
 CC and multiple sclerosis. In addition, the protein and its gene can be used
 CC to prevent apoptosis following organ transplantation.
 CC Note: The present sequence is not shown in the specification but is
 CC derived from the Homo sapiens wild-type FLINT sequence shown on page
 CC 91-93 (AAB03621).
 CC
 XX
 SQ Sequence 300 AA;
 Query Match 92.4%; Score 1509; DB 21; Length 300;
 Best Local Similarity 91.7%; Pred. No. 1,1e-11;
 Matches 275; Conservative 8; Mismatches 17; Indels 0; Gaps 0;

QY 1 MRALEGSLTCLIVLALPALLPYAVRGVAETPTVWRAETGERLVCAQCPPTFFVOR 60
 1 MRALEGSLTCLIVLALPALLPYAVRGVAETPTVWRAETGERLVCAQCPPTFFVOR 60

Db 1 MRALEGSLTCLIVLALPALLPYAVRGVAETPTVWRAETGERLVCAQCPPTFFVOR 60

QY 61 PCRDRSPFTGCPGPPRRYVTFWYVLERCRCNVLCGRREARACHATNRACRGTGF 120
 61 PCRDRSPFTGCPGPPRRYVTFWYVLERCRCNVLCGRREARACHATNRACRGTGF 120

Db 61 PCRDRSPFTGCPGPPRRYVTFWYVLERCRCNVLCGRREARACHATNRACRGTGF 120

QY 121 AHAGFCLHASCPCGAGVIAPTPSONTCQCPPTGFSASSSSSECCQPHRNCATLGLA 180
 121 AHAGFCLHASCPCGAGVIAPTPSONTCQCPPTGFSASSSSSECCQPHRNCATLGLA 180

Db 121 AHAGFCLHASCPCGAGVIAPTPSONTCQCPPTGFSASSSSSECCQPHRNCATLGLA 180

| | | | |
|----|-------------------------|---------------|---|
| FT | Misc-difference | 33 | /note= "wild-type Thr substituted by Ala, Ser, Gly, Leu, Val or Ile" |
| FT | Misc-difference | 41 | /note= "wild-type Ala substituted by Thr, Gly, Val, Leu or Ile" |
| FT | Misc-difference | 42 | /note= "wild-type Glu substituted by Asn or Gln" |
| FT | Domain | 43..85 | /label= domain_2 |
| FT | Misc-difference | 46 | /note= "wild-type Arg substituted by His or Lys" |
| FT | Misc-difference | 60 | /note= "wild-type Arg substituted by His or Lys" |
| FT | Domain | 86..112 | /label= domain_3 |
| FT | Misc-difference | 104 | /note= "wild-type Ala substituted by Gly, Val, Leu or Ile" |
| FT | Domain | 123..165 | /label= domain_4 |
| FT | Misc-difference | 131 | /note= "wild-type Ser substituted by Leu, Thr, Ile, Ala or Gly" |
| FT | Misc-difference | 136 | /note= "wild-type Ala substituted by Gly, Val, Leu or Ile" |
| FT | Misc-difference | 139 | /note= "wild-type Ile substituted by Leu, Gly, Ala or Val" |
| FT | Misc-difference | 191 | /note= "wild-type Thr substituted by Ala, Ser, Gly, Leu, Ile or Val" |
| FT | Misc-difference | 198 | /note= "wild-type Gly substituted by Ala, Val, Ile or Leu" |
| FT | Misc-difference | 208 | /note= "wild-type Ala substituted by Gly, Leu, Val or Ile" |
| FT | Misc-difference | 212 | /note= "wild-type Glu substituted by Asp, Asn or Gln" |
| FT | Misc-difference | 238 | /note= "wild-type Ala substituted by Gly, Leu, Val or Ile" |
| FT | Misc-difference | 254 | /note= "wild-type Glu substituted by Arg, Asn, Asp, Glu, Lys or His" |
| FT | Misc-difference | 258 | /note= "wild-type Arg substituted by Gln, Lys, His, Asn, Asp or Glu" |
| FT | Misc-difference | 259 | /note= "wild-type Arg substituted by Gln, Lys, His, Asn, Asp or Glu" |
| FT | Misc-difference | 266 | /note= "wild-type Gly substituted by Glu, Asn, Gln, Ala, Val, Leu, Ile or Asp" |
| FT | Misc-difference | 299 | /note= "wild-type Val substituted by Gly, Leu, Ile or Ala" |
| XX | WO200034782-A1. | | |
| PD | 15-JUN-2000. | | |
| XX | 07-DEC-1999; | 99WO-D528696. | |
| XX | 09-DEC-1998; | 98US-O111575. | |
| PR | 09-DEC-1998; | 98US-O111580. | |
| PR | 07-JAN-1999; | 99US-O115069. | |
| XX | (ELIL) LILLY & CO ELI. | | |

| | |
|---|---|
| PI | Rosteck PRJ., Song HY, Su EW; |
| XX | |
| DR | WPI: 2000-431379/37. |
| PT | Novel monkey Fas ligand inhibitor polypeptides, useful for treating |
| PT | inflammatory or autoimmune disease such as rheumatoid arthritis, |
| PT | infectious diseases such as chronic hepatitis, and |
| PT | Ischaemia/Re-perfusion conditions - |
| PS | Claim 3; Page -: 101pp; English. |
| XX | |
| CC | The present sequence is a mutant protein sequence of the human Fas |
| CC | ligand inhibitor (FLINT). The FLINT protein is involved in cell-specific |
| CC | apoptosis, and can be used to treat inflammatory and autoimmune diseases |
| CC | such as rheumatoid arthritis, inflammatory bowel disease, |
| CC | graft-versus-host disease, diabetes, psoriasis and Graves' disease, |
| CC | infectious diseases such as HIV-induced lymphopenia, fulminant viral |
| CC | hepatitis B/C, chronic hepatitis and cirrhosis, and H. pylori-associated |
| CC | ulceration, ischemia and reperfusion conditions including acute |
| CC | myocardial infarction, acute coronary syndrome, congestive heart failure |
| CC | and atherosclerosis, and Alzheimer's and Parkinson's diseases, acute |
| CC | lung injury and acute respiratory distress syndrome, Crohn's disease, |
| CC | brain trauma and injury, chronic glomerulonephritis, osteoporosis, |
| CC | aplastic anaemia, myelodysplasia, ulcerative colitis, Down's syndrome, |
| CC | and multiple sclerosis. In addition, the protein and its gene can be used |
| CC | to prevent apoptosis following organ transplantation. |
| CC | Note: The present sequence is not shown in the specification but is |
| CC | derived from the Homo sapiens wild-type FLINT sequence shown on page |
| CC | 91-93 (AAB03621). |
| XX | |
| SQ | Sequence 300 AA: |
| | |
| Query Match | 91.9%; Score 1502; DB 21; Length 300; |
| Best Local Similarity | 91.7%; Pred. No. 4e-111; |
| Matches 275; Conservative 0; Mismatches 25; Indels 0; Gaps 0; | |
| OY | 1 MRALEPGSLILCLYLALPALLPVAVGVAEPTPYPRKDAETGGRLYCAQCPEGTFFQR 60 |
| DB | 1 MRALEGPGLILCLIXALPALLVYVAXGXEXEPYPWRDXXTGXELCACCPPTFVOX 60 |
| OY | 61 PCRRDSPYTTCGPCPPRHNTQFWNVYERRCNCVLGGEFEERARACHATHNRACRGTGF 120 |
| DB | 61 PCRDSPTTGCPCPPRHNTQTWNMYLERCRYCNVLGGEFEERARKAHATHNRCRTFTFF 120 |
| OY | 121 AHAGFCLHEASCPPGAGVIAPGTPSQNTQCPCPPGTFSASSSSSEDCQPHRNCTALGLA 180 |
| DB | 121 AHAGFCLHEAACPPEGXVAPGTPSQNTQCPCPGTFSASSSSSEDCQPHRNCTALGLA 180 |
| OY | 181 LNVPGSSSHDPLTLCSTCTGFPSTRPGAGEECBRAVIDVAADODISIKRLORLQALEAPE 240 |
| DB | 181 LNVPGSSSHDLTLCTSTCFPLSTRPGAGECXRAVIDVAADODISIKRLORLQALEAPE 240 |
| OY | 241 GMGPFPFRGRALQLKLRRLTELLGAODGALVRLQALRVARNRPFGERSVREFFLVH 300 |
| DB | 241 GMGPFPFRGRALKLKXKRITELLXAODGALLVRLQALRVARNRPFGERSVREFFLPXH 300 |
| RESULT 39 | |
| ID | AAY42184 |
| XX | AAY42184 standard; Protein: 271 AA. |
| AC | AAY42184; |
| XX | |
| DT | 17-DEC-1999 (first entry) |
| XX | |
| DE | Human mFLINT #1 protein sequence. |
| XX | |
| KW | Human; FLINT; mFLINT; OPG3; tumour necrosis factor receptor; FasL; |
| KW | apoptosis; inflammation; cancer; diabetes; acute liver failure; |
| KW | sepsis; hepatitis; ischaemia-associated injury; hypercoagulation; |
| KW | reperfusion-associated injury; aplastic anemia; differentiation; |
| KW | growth; myelodysplastic syndrome; pancytopenic condition; |
| KW | myocardial ischaemia. |

| | |
|-----------------------|---|
| XX | Homo sapiens. |
| OS | |
| XX | |
| XX | MO9950413-A2. |
| PN | |
| XX | |
| PD | 07-OCT-1999. |
| XX | |
| PE | 30-MAR-1999; 99WO-US06797. |
| PR | |
| XX | 30-MAR-1998; 98US-0079856. |
| PR | 20-MAY-1998; 98US-0086074. |
| PR | 09-SEP-1998; 98US-0099643. |
| PR | 17-DEC-1998; 98US-0112577. |
| PR | 18-DEC-1998; 98US-0112703. |
| PR | 18-DEC-1998; 98US-0112933. |
| PR | 22-DEC-1998; 98US-0113407. |
| XX | |
| PA | (EULI) LILLY & CO ELI. |
| PI | Bumol TF, Dou S, Glasebrook AL, Gould KE, Hale JE, Heuer JS; |
| PI | Hui KY, Khatibnashov A, Mizrahi J, Na S., Noblitt TW, Reidy CA; |
| PI | Song HY, Wang J, Wu X, Zuckerman SH; |
| DR | WPI: 1999-591319/50. |
| DR | N-PsDB: AAZ25377. |
| PT | Use of mature FLINT for treating acute liver failure, inflammation, |
| PT | cancer, and diabetes - by prevention of FasL-Fas mediated apoptotic |
| PT | and proinflammatory activity |
| XX | |
| XX | Claim 31, Fig 3; 99pp; English. |
| XX | |
| CC | The present invention describes therapeutic applications of mature FLINT |
| CC | (mFLINT) for use in the treatment of acute liver failure. Mature FLINT |
| CC | (mFLINT), which is a member of the tumour necrosis factor receptor |
| CC | superfamily, is used for treating acute liver failure, inflammation of |
| CC | the liver, abnormal hepatocyte apoptosis, sepsis, a disorder associated |
| CC | with inflammation, hepatitis, abnormal apoptosis, an ischemia-associated |
| CC | injury or disorder such as hypercoagulation (including use with |
| CC | thrombolytic or anti-thrombolytic agents), reperfusion-associated injury |
| CC | or disorder, Type I diabetes, cancer, cell damage or damage to an |
| CC | innocent bystander tissue that is induced by a chemotherapeutic agent or |
| CC | therapeutic irradiation, treating haematopoietic progenitor cells that |
| CC | have been exposed to therapeutic radiation or chemotherapy, aplastic |
| CC | anemia, myelodysplastic Syndrome or a pancytopenic condition. mFLINT is |
| CC | also used for promoting the growth or differentiation of a haematopoietic |
| CC | progenitor cell or CD34+ cell and preventing damage to a cardiac myocyte |
| CC | resulting from abnormal myocardial ischaemia. The present sequence |
| CC | represents human mFLINT. |
| XX | |
| XX | Sequence 271 AA: |
| Query Match | 91.2%; Score 1491; DB 20; Length 271; |
| Best Local Similarity | 100.0%; Pred. No. 2.7e-110; |
| Matches 271: | Conservative 0; Mismatches 0; Indels 0; Gaps 0 |
| OY | 30 VAEPTPYPMWRDAETGGERLVCAQCPGGTFVORPCRRDSEPTTGCPPRHYYTOFWNYLERCR 89 |
| Dd | 1 VAEPPTYWMRDAETGGERLVCAQCPGGTFVORPCRRDSEPTTGCPPRHYYTOFWNYLERCR 60 |
| OY | 90 YCNVLGGREREDEARACHATHNRACRCRTGFFAHAGFCLEHASCPGAGVIAPGPSOMTU 149 |
| Dd | 61 YCNVLGGREREDEARACHATHNRACRCRTGFFAHAGFCLEHASCPGAGVIAPGPSOMTU 120 |
| OY | 150 CQCPPGGFGSSASSSSSBOCOPHRNTALGIALNVGSSSHDTLCISCGFPLSTRVPAGE 209 |
| Dd | 121 CQCPPGGFGSSASSSSSBOCOPHRNTALGIALNVGSSSHDTLCISCGFPLSTRVPAGE 180 |
| OY | 210 ECEBAVIDEFVAFODISIKRLQRLQALEAPBEGMTPPAGRAALDLKLRRLTELLGAOD 269 |
| Dd | 181 ECERAVIDEFVAFODISIKRLQRLQALEAPBEGMTPPAGRAALDLKLRRLTELLGAOD 240 |
| OY | 270 GALLVRLLQALRVARMGLERSVRERLPVH 300 |

| Db | 241 | GALVLRLLQALNRVARRPAGLERSVRRFLPVH | 271 |
|----------|---|--|-----|
| RESULT | 40 | | |
| AAB19334 | | | |
| ID | AAB19334 | standard; Protein: 271 AA. | |
| XX | | | |
| AC | AAB19334; | | |
| XX | | | |
| DT | 19-FEB-2001 | (first entry) | |
| XX | | | |
| DE | A mature human FAS Ligand Inhibitory Protein (FLINT). | | |
| XX | | | |
| KW | Human; FAS Ligand Inhibitory Protein; FLINT; analogue; apoptosis; | | |
| KW | tumour necrosis factor receptor; acute lung injury; pulmonary fibrosis; | | |
| KW | acute respiratory distress syndrome; ulcerative colitis; | | |
| KW | chronic obstructive pulmonary disease; Crohn's disease. | | |
| XX | | | |
| OS | Homo sapiens. | | |
| XX | | | |
| Key | Location/Qualifiers | | |
| FT | Misc-difference 1 | /note= "optionally replaced with Met" | |
| FT | Misc-difference 2 | /note= "optionally replaced with Asn" | |
| FT | Misc-difference 4 | /note= "optionally replaced with Ala" | |
| FT | Misc-difference 12 | /note= "optionally replaced with Asn" | |
| FT | Misc-difference 13 | /note= "optionally replaced with Asp or Gln" | |
| FT | Misc-difference 17 | /note= "optionally replaced with Trp" | |
| FT | Misc-difference 25 | /note= "optionally replaced with Asn" | |
| FT | Misc-difference 34 | /note= "optionally replaced with Asn" | |
| FT | Misc-difference 35 | /note= "optionally replaced with Asn" | |
| FT | Misc-difference 36 | /note= "optionally replaced with Thr" | |
| FT | Misc-difference 37 | /note= "optionally replaced with Asn or Thr" | |
| FT | Misc-difference 38 | /note= "optionally replaced with Asn" | |
| FT | Misc-difference 53 | /note= "optionally replaced with Asp" | |
| FT | Misc-difference 63 | /note= "optionally replaced with Trp" | |
| FT | Misc-difference 67 | /note= "optionally replaced with Asp" | |
| FT | Misc-difference 69 | /note= "optionally replaced with Glu" | |
| FT | Misc-difference 75 | /note= "optionally replaced with Pro" | |
| FT | Misc-difference 82 | /note= "optionally replaced with Glu or Thr" | |
| FT | Misc-difference 88 | /note= "optionally replaced with Pro" | |
| FT | Misc-difference 94 | /note= "optionally replaced with Tyr" | |
| FT | Misc-difference 95 | /note= "optionally replaced with Asp" | |
| FT | Misc-difference 96 | /note= "optionally replaced with Gln" | |
| FT | Misc-difference 101 | /note= "optionally replaced with Thr" | |
| FT | Misc-difference 102 | /note= "optionally replaced with Leu" | |
| FT | Misc-difference 104 | /note= "optionally replaced with Ser" | |
| FT | Misc-difference 107 | /note= "optionally replaced with Ser" | |

FT /note= "optionally replaced with Ser, Asp, Glu or Thr"
 FT Misc-difference 110
 FT /note= "optionally replaced with Met, Thr or Glu"
 FT Misc-difference 114
 FT /note= "optionally replaced with Asn"
 FT Misc-difference 115
 FT /note= "optionally replaced with Asn"
 FT Misc-difference 126
 FT /note= "optionally replaced with Asn"
 FT Misc-difference 132
 FT /note= "optionally replaced with Asn"
 FT Misc-difference 134
 FT /note= "optionally replaced with Thr"
 FT Misc-difference 162
 FT /note= "optionally replaced with Ala"
 FT Misc-difference 166
 FT /note= "optionally replaced with Asn"
 FT Misc-difference 169
 FT /note= "optionally replaced with Ala"
 FT Misc-difference 171
 FT /note= "optionally replaced with Asn"
 FT Misc-difference 172
 FT /note= "optionally replaced with Asn"
 FT Misc-difference 179
 FT /note= "optionally replaced with Thr"
 FT Misc-difference 183
 FT /note= "optionally replaced with Lys"
 FT Misc-difference 194
 FT /note= "optionally replaced with Asn"
 FT Misc-difference 196
 FT /note= "optionally replaced with Thr"
 FT Misc-difference 209
 FT /note= "optionally replaced with Thr"
 FT Misc-difference 225
 FT /note= "optionally replaced with Arg"
 FT Misc-difference 237
 FT /note= "optionally replaced with Glu"
 FT Misc-difference 270
 FT /note= "optionally replaced with Gly"
 PN WO200058465-A2.
 PD 05-OCT-2000.
 XX
 PF 20-MAR-2000; 2000MO-US06417.
 XX
 PR 30-MAR-1999; 99US-0126839.
 PR 21-JUN-1999; 99US-0140077.
 PR 21-JUN-1999; 99US-0140156.
 PR 20-OCT-1999; 99US-0160366.
 PR 18-FEB-2000; 2000US-0183398.
 XX
 XX (ELIL) LILLY & CO ELI.
 PI Becker GW, Cohen FT, Gonzalez-dewhitt PA, Hale JE, Micanovic R;
 PI Newton CM, Noblitt TW, Ratnamachalam R, Tschang SR, Witcher DR;
 PI Wroblewski VJ;
 XX
 DR WPI; 2000-656167/63.
 DR N-PSDB; AAA75999.
 XX
 PT FAS ligand Inhibitory Protein analogs useful for treating abnormal
 PT apoptosis related diseases e.g. acute lung injury, pulmonary fibrosis,
 PT chronic obstructive pulmonary disease ulcerative colitis or Crohn's
 PT disease
 XX
 PS Claim 1; Page 112-113; 114pp; English.
 CC
 CC The present sequence represents a mature human FAS ligand Inhibitory
 CC Protein (FLINT). FLINT is a homologue of tumour necrosis factor receptor
 CC proteins. FLINT inhibits the binding of FAS to FAS ligand. The mature
 CC FLINT protein is modified to produce analogues, which have greater
 CC potency, longer in vivo half-lives, decreased aggregation, decreased

CC absorption onto surfaces, increased solubility and improved ease of
 CC formulation. The FLINT analogue is useful for treating a patient
 CC suffering from disease or condition relating to abnormal apoptosis such
 CC as acute lung injury, acute respiratory distress syndrome, pulmonary
 CC fibrosis, chronic obstructive pulmonary disease, ulcerative colitis, or
 CC Crohn's disease.
 CC
 XX Sequence 271 AA;
 SQ
 Query Match 91.2%; Score 1491; DB 21; Length 271;
 Best Local Similarity 100.0%; Pred. No. 2.7e-110;
 Matches 271; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 30 VAETPTPMWDAETGERLVCAQCPPTGVORPCRRSDPTTCGPPRHYYTFQMYLRCR 89
 DB 1 VAETPTPMWDAETGERLVCAQCPPTGVORPCRRSDPTTCGPPRHYYTFQMYLRCR 60
 QY 90 YCNVLCGEREBEARACHATNHRACRRTGFPANAFCLEHASCPGAGVIAPTPSQNTQ 149
 DB 61 YCNVLCGEREBEARACHATNHRACRRTGFPANAFCLEHASCPGAGVIAPTPSQNTQ 120
 QY 150 CQPCPPTFSASSSSSSFCOCPPHRCCTALGALANVPGSSSHDTCTCTGFPPLSTRVGA 209
 DB 121 CQPCPPTFSASSSSSSFCOCPPHRCCTALGALANVPGSSSHDTCTCTGFPPLSTRVGA 180
 QY 210 ECERAVIDFAFODISIKRLQRLQALEAEGMGPPRAGRALQTLRRRLTELLGAQD 269
 DB 181 ECERAVIDFAFODISIKRLQRLQALEAEGMGPPRAGRALQTLRRRLTELLGAQD 240
 QY 270 GALLVRLQALRAVMGELRSVEREPLPVH 300
 DB 241 GALLVRLQALRAVMGELRSVEREPLPVH 271
 Db
 RESULT 41
 AAB19705
 ID AAB19705 standard; Protein; 271 AA.
 XX
 XX AAB19705;
 DT 05-FEB-2001 (first entry)
 XX
 DE Human FAS ligand inhibitor protein FLINT.
 XX
 KW FLINT; FAS ligand inhibitory protein; human; protease resistant;
 KW acute lung injury; acute respiratory distress syndrome;
 KW chronic obstructive pulmonary disease; pulmonary fibrosis;
 KW ulcerative colitis; therapy; organ transplantation.
 XX
 OS Homo sapiens.
 XX
 FH Key Location/Qualifiers
 FT Cleavage-site 218..219
 FT /note= "cleaved by trypsin-like proteases"
 FT Misc-difference 34
 FT /note= "optionally replaced by Arg, as given in
 FT Claims 10, 11, 13 and 14"
 FT Misc-difference 36
 FT /note= "optionally replaced by Thr, as given in
 FT Claims 10, 11, 13 and 14"
 FT Misc-difference 132
 FT /note= "optionally replaced by Asn, as given in
 FT Claim 12"
 FT Misc-difference 194
 FT /note= "optionally replaced by Asn, as given in
 FT Claims 11 and 14"
 FT Misc-difference 196
 FT /note= "optionally replaced by Thr, as given in
 FT Claims 11 and 14"
 FT Misc-difference 214
 FT /note= "optionally replaced by any naturally
 FT occurring amino acid"
 FT Misc-difference 215

ET /note= "optionally replaced by any naturally occurring amino acid"

ET Misc-difference 216 /note= "optionally replaced by any naturally occurring amino acid, preferably Pro as given in Claims 9 and 15"

ET Misc-difference 217 /note= "optionally replaced by any naturally occurring amino acid, preferably Tyr as given in Claim 9"

ET Misc-difference 218 /note= "optionally replaced by any naturally occurring amino acid, preferably Gln, Glu, Ala, Gly, Ser, Val, Tyr or Asn as given in Claims 9, 10, 11, 12, especially Gln as given in Claims 13, 14, 15, 35 and 36"

ET Misc-difference 219 /note= "optionally replaced by any naturally occurring amino acid"

ET Misc-difference 220 /note= "optionally replaced by any naturally occurring amino acid"

ET Misc-difference 221 /note= "optionally replaced by any naturally occurring amino acid"

ET Misc-difference 222 /note= "optionally replaced by any naturally occurring amino acid"

ET WO200058466-A2.

PN 05-OCT-2000.

PD 20-MAR-2000; 2000WO-US06418.

PE 30-MAR-1999; 99US-0126839.

PR 21-JUN-1999; 99US-0140073.

PR 04-AUG-1999; 99US-0147071.

PR 20-OCT-1999; 99US-0160524.

PR 21-OCT-1999; 99US-0160669.

PR 20-DEC-1999; 99US-0172744.

PR 26-JAN-2000; 2000US-0178184.

XX (ELIL) LILLY & CO ELI.

PA Micanovic R, Rathnachalam R, Witcher DR;

XX WPI: 2000-664925/64.

DR N-PSDB: AAA88730.

XX Novel protease resistant FAS ligand inhibitory protein analogues resistant to in vivo or in vitro proteolysis at amino acid position 218 of the mature protein, useful for treating autoimmune diseases

PT Claim 1: Page 94-95; 100pp; English.

XX The present sequence is that of human FAS ligand inhibitory protein FLINT mature protein. FLINT is a tumour necrosis factor receptor homologue that binds FAS ligand, preventing its interaction with FAS. This interaction is implicated in runaway apoptosis and inflammatory disease. FLINT also binds to LIGHT, a membrane-bound ligand, which may play a role in immune modulation and apoptosis. The invention relates to novel FLINT analogues (see also AAB19706-09) that are resistant to proteolysis by trypsin-like proteases between positions 218 and 219 of the FLINT mature protein sequence. The analogues have amino acid substitutions in the region comprising amino acids 214-222, and may contain additional substitutions at residues 34, 36, 132, 194 and/or 196. Nucleic acids, vectors and transformed host cells for recombinant production of the analogues are claimed. FLINT cDNA (see AAA88730) is used as a template for introducing the required point mutations. The protease resistant FLINT analogues are used to prevent or treat acute lung injury, acute respiratory stress syndrome, ulcerative colitis, chronic

CC obstructive pulmonary disease, pulmonary fibrosis, to inhibit T lymphocyte activation, and to facilitate organ preservation for transplantation (claimed).

CC transplanted organ (claimed).

XX SQ Sequence 271 AA:

Query Match 91.2%; Score 1491; DB 21; Length 271;

Best Local Similarity 100.0%; Pred. No. 2,7e-110;

Matches 271; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 30 VAETPPYPMRDAETGERLVCAQCPGTFVQRPCCRRDSTTCGPPRRHYTFWMYLERCR 89

DB 1 VAETPPYPMRDAETGERLVCAQCPGTFVQRPCCRRDSTTCGPPRRHYTFWMYLERCR 60

QY 90 YCNVLCGRREDEARACHTHNRACRCRGFFAHAGFCLEHNSCPGAGAVIAPGPSQMTQ 149

DB 61 YCNVLCGRREDEARACHTHNRACRCRGFFAHAGFCLEHNSCPGAGAVIAPGPSQMTQ 120

QY 150 COPCPPTFSASSSSSECCOPHRNCTALGLALNVPSSSDTLCTSGTFPLSTPVPAGAE 209

DB 121 COPCPPTFSASSSSSECCOPHRNCTALGLALNVPSSSDTLCTSGTFPLSTPVPAGAE 180

QY 210 ECERAVIDFVAFODISIKRLQRLQALPAPEGWGPPTPAGRAALQKLRRLTELLGAQD 269

DB 181 ECERAVIDFVAFODISIKRLQRLQALPAPEGWGPPTPAGRAALQKLRRLTELLGAQD 240

QY 270 GALVRLQLARVARMPELERSVRRFLPVH 300

DB 241 GALVRLQLARVARMPELERSVRRFLPVH 271

RESULT 42

AA97247

ID AA97247 standard; Protein; 271 AA.

XX AA97247;

AC 19-DEC-2000 (first entry)

XX M68 TNF receptor related protein (mature protein).

DE M68: tumour necrosis factor; TNF; programmed cell death; apoptosis; receptor; immune response; cell differentiation; ligand; cancer; bone disease; systemic lupus erythematosus; Hashimoto's thyroiditis; Grave's disease; idiopathic myxedema; autoimmune diabetes; thrombotic thrombocytopenic purpura; multiple sclerosis; liver diseases; autoimmune gastritis; ulcerative colitis; glomerulonephritis; pulmonary fibrosis; heart failure; atherosclerosis; aplastic anaemia; myelodysplastic syndromes; osteoporosis; Alzheimer's disease; Parkinson's disease; stroke; myocardial infarction; human.

XX Homo sapiens.

OS WO200046247-A1.

XX 10-AUG-2000.

PD 04-FEB-2000; 2000WO-US03037.

XX 05-FEB-1999; 99US-0118902.

PR 20-DEC-1999; 99US-0172754.

XX (MERI) MERCK & CO INC.

PA Bai C;

XX WPI: 2000-506066/45.

DR Isolated human M68 nucleic acids and proteins which are part of the tumor necrosis factor receptor (TNFR) family, useful for identifying modulators that may be used to treat various diseases e.g. cancer, osteoporosis, Alzheimer's disease

XX Claim 1; Page 76; 80pp; English.

PS The M68 protein is a member of a family of proteins which have

XX roles in immune responses, cell death, cell proliferation and

CC stimulation of cell differentiation. M68 lacks a transmembrane domain

CC and is a secreted factor suggesting that it functions as a natural

CC inhibitor for its ligand. The altered expression pattern of M68 in a

CC multitude of tissues suggests that M68 may play a role in cancer by

CC binding to its ligand and blocking apoptotic cell death induced by

CC such a ligand. This anti-apoptotic role of M68 suggests that

CC modulators of M68 will be useful in treatment of apoptosis-related

CC diseases such as various forms of cancer and various bone disorders.

CC M68 nucleic acids and proteins are therefore useful for treating

CC conditions involving atypical apoptosis and for identifying

CC modulators of M68. Modulators of M68 are useful for treatment of

CC cancer and other diseases associated with abnormal levels of

CC apoptosis including systemic lupus erythematosus, Hashimoto's

CC thyroiditis, Grave's disease, idiopathic myxedema, autoimmune

CC diabetes, thrombotic thrombocytopenic purpura, multiple sclerosis,

CC liver diseases, autoimmune gastritis, ulcerative colitis,

CC glomerulonephritis, pulmonary fibrosis, heart failure,

CC atherosclerosis, aplastic anaemia, myelodysplastic syndromes,

CC osteoporosis, Alzheimer's disease, Parkinson's disease, stroke, and

CC myocardial infarction.

XX Sequence 271 AA:

5Q

Query Match 91.2%; Score 1491; DB 21; Length 271;

Best Local Similarity 100.0%; Pred. No. 2.7e-110;

Matches 271; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 30 VAETPTYPWRDAEGERLYVCAQCPGTFVQRPGRDSTPTGCPPRHYTOFNNYLERCR 89

DB 1 VAETPTYPWRDAEGERLYVCAQCPGTFVQRPGRDSTPTGCPPRHYTOFNNYLERCR 60

QY 90 YCNVLGGEREEBARACHATHNRACRRTGFFAHAGFCLFELHASCPPGAGVIAPGTSQNTQ 149

DB 61 YCNVLGGEREEBARACHATHNRACRRTGFFAHAGFCLFELHASCPPGAGVIAPGTSQNTQ 120

QY 150 CQPCPPGTFSSASSSSSECCQPHRNCCTALGLALNVPSSSHDTLCTSGTGFPLSTRVPGAE 209

DB 121 CQPCPPGTFSSASSSSSECCQPHRNCCTALGLALNVPSSSHDTLCTSGTGFPLSTRVPGAE 180

QY 210 ECERAVIDEFAFODISIKRLQRLQALFAPBEGMGPTPRAGRAALQKLRRLTELLGAOD 269

DB 181 ECERAVIDEFAFODISIKRLQRLQALFAPBEGMGPTPRAGRAALQKLRRLTELLGAOD 240

QY 270 GALLVRLQLQALRVAMPGLERSVEREFLPVH 300

DB 241 GALLVRLQLQALRVAMPGLERSVEREFLPVH 271

RESULT 43

AAE03567

ID AAY96598 standard; Protein; 271 AA.

XX AAY96598;

AC

XX 26-SEP-2000 (first entry)

DT

XX

DE Human mature FLINT.

XX

XX FLINT; osteoprotegerin 3; OPG3; tumour necrosis factor receptor; TNFR;

KW FasL; LIGHT; apoptosis; pro-inflammatory; hepatotropic; vasotropic;

KM anti-diabetic; anti-anaemic; neuroprotective; anti-ulcer; cytoskeletal;

XX anti-inflammatory; antibacterial; immunosuppressive.

OS Homo sapiens.

XX

XX WO200037094-AZ.

PN

XX

PD 29-JUN-2000.

XX 21-DEC-1999; 99WO-US30734.

PF

XX 22-DEC-1998; 98US-0113407.

XX

PR 30-MAR-1999; 99WO-US06797.

PR

XX 20-OCT-1999; 99US-0172239.

XX

PA (EHL) LILLY & CO ELI.

XX

PI Cohen FJ, Posada JA, Wierda D;

XX

DR WPI: 2000-475441/41.

XX

DR N-PSDB; AAA51077.

XX

PS Use of mature FLINT for treating e.g. acute respiratory distress

PT syndrome, ulcerative colitis or ischemic injury during organ

PT transplantation

XX

XX Example 8; Fig 3; 125pp; English.

XX

XX Human FLINT (also known as osteoprotegerin 3) is a new tumour necrosis

CC factor receptor (TNFR) superfamily member, which binds FasL and LIGHT and

CC prevents FasL-Fas interaction. Mature FLINT (mFLINT) inhibits FasL-Fas

CC mediated apoptotic and pro-inflammatory activity. mFLINT is useful for

CC treating acute respiratory distress syndrome, treating or inhibiting

CC ulcerative colitis, inhibiting ischemic injury during organ

CC transplantation or for organ preservation during transplantation. mFLINT

CC can also be used to treat acute liver failure, inflammation of the liver,

CC abnormal (hepatocyte) apoptosis, sepsis, disorders associated with

CC inflammation, hepatitis, ischemia, hypercoagulation or reperfusion,

CC damage to a cardiac myocyte resulting from abnormal myocardial ischemia,

CC Type 1 diabetes, cancer, damage to an innocent bystander tissue induced

CC by a chemotherapeutic or therapeutic irradiation, aplastic anaemias,

CC myelodysplastic syndromes and pancytopenic conditions.

XX

5Q Sequence 271 AA:

Query Match 91.2%; Score 1491; DB 21; Length 271;

Best Local Similarity 100.0%; Pred. No. 2.7e-110;

Matches 271; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 30 VAETPTYPWRDAEGERLYVCAQCPGTFVQRPGRDSTPTGCPPRHYTOFNNYLERCR 89

DB 1 VAETPTYPWRDAEGERLYVCAQCPGTFVQRPGRDSTPTGCPPRHYTOFNNYLERCR 60

QY 90 YCNVLGGEREEBARACHATHNRACRRTGFFAHAGFCLFELHASCPPGAGVIAPGTSQNTQ 149

DB 61 YCNVLGGEREEBARACHATHNRACRRTGFFAHAGFCLFELHASCPPGAGVIAPGTSQNTQ 120

QY 150 CQPCPPGTFSSASSSSSECCQPHRNCCTALGLALNVPSSSHDTLCTSGTGFPLSTRVPGAE 209

DB 121 CQPCPPGTFSSASSSSSECCQPHRNCCTALGLALNVPSSSHDTLCTSGTGFPLSTRVPGAE 180

QY 210 ECERAVIDEFAFODISIKRLQRLQALFAPBEGMGPTPRAGRAALQKLRRLTELLGAOD 269

DB 181 ECERAVIDEFAFODISIKRLQRLQALFAPBEGMGPTPRAGRAALQKLRRLTELLGAOD 240

QY 270 GALLVRLQLQALRVAMPGLERSVEREFLPVH 300

DB 241 GALLVRLQLQALRVAMPGLERSVEREFLPVH 271

RESULT 44

AAE03567

ID AAE03567 standard; Protein; 271 AA.

XX AAE03567;

AC

XX 04-AUG-2001 (first entry)

DT

XX

DE Human mature fas ligand inhibitory protein (FLINT).

XX

XX Human; fas ligand inhibitory protein; FLINT; acute lung injury; ALI;

| | | |
|----|---|--|
| KM | TNFR: | tumour necrosis factor receptor protein; ulcerative colitis; ARDS, |
| KM | acute | respiratory distress syndrome; pulmonary fibrosis; pr; therapy; |
| KM | chronic | obstructive pulmonary disease; COPD; acute lung injury; goitre; |
| KM | rheumatoid | arthritis; fibroproliferative lung disease; ischemia; sepsis; |
| KM | fibrotic | lung diseases; human immunodeficiency virus; HIV; osteoporosis; |
| KM | chronic | renal failure; graft-vs-host disease; cutaneous inflammation; |
| KM | vascular | leak syndrome; Helicobacter pylori infection; atherosclerosis; |
| KM | insulin | dependent diabetes mellitus (IDDM); inflammatory bowel disease; |
| KM | Crohn's | disease; pancreatitis; cancer; autoimmune disease; psoriasis; |
| KM | Down's | syndrome; multiple sclerosis; cytostatic; noctropic; |
| KM | neuroprotective; | vasotropic. |
| OS | Homo sapiens. | |
| XX | | |
| XX | Key | location/Qualifiers |
| FT | Modified-site | 144 |
| FT | | /note= "N-linked glycosylation site" |
| FT | Modified-site | 174 |
| FT | | /note= "O-linked glycosylation site" |
| FT | Modified-site | 216 |
| FT | | /note= "O-linked glycosylation site" |
| FT | Cleavage-site | 218..219 |
| FT | | /note= "Proteolytic cleavage" |
| XX | | |
| XX | WO200142463-A1. | |
| XX | 14-JUN-2001. | |
| PD | | |
| XX | 29-NOV-2000; | 2000MO-US30166. |
| PF | | |
| XX | 07-DEC-1999; | 990S-0169367. |
| XX | 07-DEC-1999; | 990S-0169381. |
| PR | 07-DEC-1999; | 990S-0169412. |
| PR | 23-MAR-2000; | 2000US-0191430. |
| XX | | |
| XX | (ELU) | LILLY & CO ELI. |
| PA | | |
| XX | | |
| PI | Lu J, Witcher DR: | |
| DR | WPI: 2001-381684/40. | |
| DR | N-PSDB; AAD07380. | |
| XX | | |
| XX | New FLINT polypeptide for treating and/or preventing acute lung injury, | |
| PT | acute respiratory distress syndrome, ulcerative colitis, and | |
| PT | graft-versus-host disease, comprises O-linked or N-linked | |
| PT | oligosaccharides - | |
| XX | | |
| PS | Example 1; Page 52-53; 60pp; English. | |
| XX | | |
| XX | The present sequence is human mature fas ligand, inhibitory protein | |
| CC | (FLINT). FLINT, a homologue of tumour necrosis factor receptor | |
| CC | protein (TNFR), binds fas ligand (FasL) and thereby preventing the | |
| CC | interaction of FasL with fas. FLINT comprising O-linked or N-linked | |
| CC | oligosaccharides is useful for preventing or treating acute lung injury | |
| CC | (ALI), acute respiratory distress syndrome (ARDS), ulcerative colitis, | |
| CC | chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis (PF), | |
| CC | to facilitate organ preservation for transplantation and to inhibit T | |
| CC | lymphocyte activation. FLINT is useful for treating and/or preventing | |
| CC | diseases such as rheumatoid arthritis, fibroproliferative lung disease, | |
| CC | fibrotic lung disease, acute lung injury, human immunodeficiency virus | |
| CC | (HIV), ischemia, brain trauma/injury, chronic renal leak syndrome, | |
| CC | Helicobacter pylori infection, goitre, atherosclerosis, insulin dependent | |
| CC | diabetes mellitus (IDDM), osteoporosis, inflammatory bowel disease, | |
| CC | Crohn's disease, sepsis, pancreatitis, cancer, autoimmune disease such as | |
| CC | psoriasis, Down's syndrome, and multiple sclerosis. | |
| XX | | |
| XX | Sequence 271 AA: | |

| | | | | |
|---|---|--|--|-----|
| Qy | | 30 | VAEPETPYPRADAEFTGSLVCAACPGTFFVORPCRPDSPTTCGCPRHYPHOEWNLYECR | 89 |
| Dd | | 1 | VAETPLYPKRDSETGERLVCACCPGTFFVQRPCRKRSPPTTCGCPPHNYTOFWNNYLERC | 60 |
| Qy | | 90 | YCNVLICGESEEEERARACHATHNRACRCRTOFFFAHAGCLSEHASCPPEAGVIAPETPSQNTQ | 149 |
| Dd | | 61 | YCNVLICGESEEEERARACHATHNRACRCRTGFPFHAAGCLSEHASCPPEAGVIAPETPSQNTQ | 120 |
| Qy | | 150 | CQCPPEPTGFSSASSSSEDQCQPHRNCTALGLALNVNPDSSSHDTLTCTSGTGPLSTRVGAE | 209 |
| Dd | | 121 | CQCPPEPTGFSSASSSSEDQCQPHRNCTALGLALNVNPDSSSHDTLTCTSGTGPLSTRVGAE | 180 |
| Qy | | 210 | ECEERAVIDPVAQAODISIKRLQRLQLALEAPEEGMGPFRAGRALQJLRRLLELLGAOD | 265 |
| Dd | | 181 | ECEERAVIDPVAQAODISIKRLQRLQLALEAPEEGMGPFRAGRALQJLRRLLELLGAOD | 240 |
| Qy | | 270 | GALLVRLLQALRVARMPLERSVREERFLPVH | 300 |
| Dd | | 241 | GALLVRLLQALRVARMPLERSVREERFLPVH | 271 |
| RESULT 45 AAB68044 ID AAB68044 standard; Protein; 271 AA. | | | | |
| XX | AC | AAB68044; | | |
| XX | DF | 29-JUN-2001 (first entry) | | |
| DE | | Amino acid sequence of a human mature FLINT polypeptide. | | |
| KW | FLINT; FAS ligand inhibitory protein; divalent metal cation; Fas; | | | |
| KW | Fas ligand; acute liver failure; cerebral ischemia; apoptosis. | | | |
| OS | Homo sapiens. | | | |
| PX | WO200118055-A1. | | | |
| XX | 15-MAR-2001. | | | |
| XX | 31-AUG-2000; 2000MO-US20807. | | | |
| XX | 10-SEP-1999; 99US-0153339. | | | |
| PA | (ELIL) LILLY & CO ELI. | | | |
| PI | Atkinson PR, Tian Y, Witcher DR; | | | |
| DR | WPI; 2001-273382/28. | | | |
| CC | Compositions comprising a divalent metal cation and a FAS ligand | | | |
| PT | Inhibitory Protein (FLINT), for reducing or inducing aggregation of | | | |
| PT | FLINT and for treating diseases involving FasL/Fas and/or | | | |
| PT | LIGHT/LT-beta R receptor interactions | | | |
| XX | Example 1; Page 39-40; 44pp; English. | | | |
| XX | The present sequence represents a mature FLINT (FAS ligand inhibitory | | | |
| CC | Protein) polypeptide. The specification describes a composition | | | |
| CC | comprising a divalent metal cation and FLINT protein. The composition | | | |
| CC | is used either for reducing, reversing or eliminating aggregation and | | | |
| CC | precipitation of FLINT or for inducing oligomerisation or aggregation | | | |
| CC | of FLINT molecules. They can be used for purifying FLINT and/or | | | |
| CC | maintaining FLINT in solution. The compositions are used to treat | | | |
| CC | and/or prevent disorders associated with the binding of Fas to FasL | | | |
| CC | and/or LIGHT to the ltbetar and/or TR2/HVEM receptors. Uses include the | | | |
| CC | treatment of acute liver failure and cerebral ischemia and the prevention | | | |
| CC | of apoptosis. | | | |
| XX | Sequence 271 AA; | | | |
| XX | | | | |
| SQ | | | | |
| Query Match | 91.2%; Score 1491; DB 22; Length 271; | | | |
| Best Local Similarity | 100.0%; Pred. No. 2.7e-110. | | | |

Matches 271: Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 30 VAETPTPMRDAETGERLVCAQCPTGTFVQPCRRDPTTCGPPPHHTQFMWYLERCR 89
1 VAETPTPMRDAETGERLVCAQCPTGTFVQPCRRDPTTCGPPPHHTQFMWYLERCR 60

QY 90 YCNVLCGEREBEABACATNHRACRCRTGFFAHAGFCLENASCPGAGVIAPTGPSQNTQ 149
61 YCNVLCGEREBEABACATNHRACRCRTGFFAHAGFCLENASCPGAGVIAPTGPSQNTQ 120

QY 150 CQPCPPTFSASSSSSSQCCPHRNCIALGLALNPGSSSHDTLCTSGTGFPLSTRVPGAE 209
121 CQPCPPTFSASSSSSSQCCPHRNCIALGLALNPGSSSHDTLCTSGTGFPLSTRVPGAE 180

QY 210 ECERAVIDFAFODISIKRLQRLQALEAPGEGMPTPRAGRAALQTLRRRLTELLGAOD 269
181 ECERAVIDFAFODISIKRLQRLQALEAPGEGMPTPRAGRAALQTLRRRLTELLGAOD 240

QY 270 GALLVRLQALRVARMGRLERSVREPLPVH 300
241 GALLVRLQALRVARMGRLERSVREPLPVH 271

Db

RESULT 46
AAB68047
ID AAB68047 standard; protein: 271 AA.
AC AAB68047;
XX
DT 29-JUN-2001 (first entry)
XX
DE Amino acid sequence of a human mature FLINT polypeptide.
XX
KW FLINT; FAS ligand inhibitory protein; divalent metal cation; Fas;
KM Fas ligand; acute liver failure; cerebral ischemia; apoptosis.
XX
OS Homo sapiens.
XX
PN W0200118041-A2.
XX
PD 15-MAR-2001.
XX
PE 31-AUG-2000; 2000MO-US20805.
XX
PR 10-SEP-1999; 99US-0153445.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Atkinson PR, Tian Y, Witcher DR;
XX
DR WPI; 2001-273381/28.
XX
XX
PT Compositions comprising a divalent metal cation and a FAS ligand
PT Inhibitory Protein (FLINT), for reducing or inducing aggregation of
PT FLINT and for treating diseases involving FasL/Fas and/or
PT LIGHT/LT-beta-R receptor interactions
XX
PS Disclosure; Page 30-31; 33pp; English.
XX
XX The present sequence represents a human mature FLINT (FAS ligand
CC Inhibitory Protein) polypeptide. The specification describes a
CC composition comprising a divalent metal cation and FLINT protein. The
CC composition is used either for reducing, reversing or eliminating
CC aggregation and precipitation of FLINT or for inducing oligomerisation
CC or aggregation of FLINT molecules. They can be used for purifying FLINT
CC and/or maintaining FLINT in solution. The compositions are used to treat
CC and/or prevent disorders associated with the binding of Fas to FasL
CC and/or LIGHT to the LtbetaR and/or TR2/HVEM receptors. Uses include the
CC treatment of acute liver failure and cerebral ischemia and the prevention
CC of apoptosis.
XX
XX Sequence 271 AA;

Query Match 91.2%; Score 1491; DB 22; Length 271;
Best Local Similarity 100.0%; Pred. No. 2.7e-110;
Matches 271: Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 30 VAETPTPMRDAETGERLVCAQCPTGTFVQPCRRDPTTCGPPPHHTQFMWYLERCR 89
1 VAETPTPMRDAETGERLVCAQCPTGTFVQPCRRDPTTCGPPPHHTQFMWYLERCR 60

QY 90 YCNVLCGEREBEABACATNHRACRCRTGFFAHAGFCLENASCPGAGVIAPTGPSQNTQ 149
61 YCNVLCGEREBEABACATNHRACRCRTGFFAHAGFCLENASCPGAGVIAPTGPSQNTQ 120

QY 150 CQPCPPTFSASSSSSSQCCPHRNCIALGLALNPGSSSHDTLCTSGTGFPLSTRVPGAE 209
121 CQPCPPTFSASSSSSSQCCPHRNCIALGLALNPGSSSHDTLCTSGTGFPLSTRVPGAE 180

QY 210 ECERAVIDFAFODISIKRLQRLQALEAPGEGMPTPRAGRAALQTLRRRLTELLGAOD 269
181 ECERAVIDFAFODISIKRLQRLQALEAPGEGMPTPRAGRAALQTLRRRLTELLGAOD 240

QY 270 GALLVRLQALRVARMGRLERSVREPLPVH 300
241 GALLVRLQALRVARMGRLERSVREPLPVH 271

Db

RESULT 47
AAB74465
ID AAB74465 standard; protein: 271 AA.
AC AAB74465;
XX
DT 30-MAY-2001 (first entry)
XX
DE Human FLINT mature protein.
XX
KW Human; FLINT; FAS ligand inhibitory protein; analogue; apoptosis;
KM Inflammatory disease.
XX
OS Homo sapiens.
XX
PN W0200118202-A2.
XX
PD 15-MAR-2001.
XX
PE 31-AUG-2000; 2000MO-US20806.
XX
PR 10-SEP-1999; 99US-0153433.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Atkinson PR, Tian Y, Witcher DR;
XX
DR WPI; 2001-257796/26.
XX
XX
PT Compositions useful for reducing/inducing aggregation of a FLINT analog
PT comprise a divalent metal cation and a protease-resistant FAS ligand
PT Inhibitory Protein (FLINT) analog
XX
PS Claim 4; Page 41-42; 44pp; English.
XX
XX The present invention describes a composition comprising a divalent metal
CC cation associated with a protease resistant Fas ligand inhibitory protein
CC (FLINT) analogue. The composition is useful in the treatment of diseases
CC associated with Fas binding to its ligand, such as acute liver failure,
CC inflammatory diseases, cerebral ischemia and apoptosis. The present
CC sequence is the mature FLINT protein.
XX
XX
XX Query Match 91.2%; Score 1491; DB 22; Length 271;
XX Best Local Similarity 100.0%; Pred. No. 2.7e-110;
XX Matches 271: Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 30 VAETPTVPMRDAETGERLVCAQCPGPTFVORPCRRDSTPTGCPCPRHYYTOFWNLECR 89
 DB 1 VAETPTVPMRDAETGERLVCAQCPGPTFVORPCRRDSTPTGCPCPRHYYTOFWNLECR 60
 QY 90 YCNVLGGEREBARACHATHNRACRCRTGFFAHAGFCLEHASCPPGAGVIAAGTSPONTQ 149
 DB 61 YCNVLGGEREBARACHATHNRACRCRTGFFAHAGFCLEHASCPPGAGVIAAGTSPONTQ 120
 QY 150 CQCPPTGTFSSASSSSSECCOPHRNCTALGLALNPVGSSSHDTLCTGTFPLSTRVPGAE 209
 DB 121 CQCPPTGTFSSASSSSSECCOPHRNCTALGLALNPVGSSSHDTLCTGTFPLSTRVPGAE 180
 QY 210 ECERAVIDFVAFODISIKRLQRLQALAPBEGMPTPRAGRAALQKLRRLTELLGAD 269
 DB 181 ECERAVIDFVAFODISIKRLQRLQALAPBEGMPTPRAGRAALQKLRRLTELLGAD 240
 QY 270 GALVRLQALRVARMPGLERSVREERFLPVH 300
 DB 241 GALVRLQALRVARMPGLERSVREERFLPVH 271

RESULT 48
 AAE14578
 ID AAE14578 standard; Protein; 271 AA.
 AC AAE14578;
 DT 01-JUL-2002 (first entry)
 XX Human mature FLINT protein.
 DE
 XX FLINT; FAS ligand inhibitory protein; pulmonary; lung; apoptosis;
 KM organ failure; liver; kidney; pancreas; inflammatory disease;
 KM neutrophil; sepsis; acute respiratory distress syndrome;
 KM acute lung injury; systemic inflammatory response syndrome; SIRS;
 KM multiple organ dysfunction; MODS; human.
 XX
 OS Homo sapiens.
 XX
 PN WO200209668-A2.
 XX
 PD 07-FEB-2002.
 XX
 PF 20-JUL-2001; 2001WO-US21105.
 XX
 PR 02-AUG-2000; 2000US-222476P.
 XX
 PA (ELIT) LILLY & CO ELI.
 XX
 PI Micranovic R, Wlitcher DR;
 XX
 DR WPI: 2002-206149/26.
 DR N-PSDB; AAD27868.
 XX
 PT Administering FLINT (FAS ligand inhibitory protein) or FLINT analog,
 PT useful for treating e.g. sepsis or respiratory distress syndrome,
 PT involves pulmonary administration of a therapeutic amount of the FLINT
 PT or FLINT analog -
 XX
 PS Disclosure: Page 29-30; 35pp; English.
 XX
 CC The invention relates to a new method of administering FLINT
 CC (FAS ligand inhibitory protein) or FLINT analog that involves pulmonary
 CC administration of a therapeutic amount of the FLINT or FLINT analog.
 CC The method enables systemic absorption of FLINT through lungs and
 CC significantly reduces or eliminates the need for administering FLINT by
 CC injection or other routes of administration. The method is useful in
 CC treating disorders related to enhanced apoptosis (e.g. organ failure
 CC in liver, kidneys and pancreas) and inflammatory diseases associated with
 CC neutrophil activation (e.g. sepsis, acute respiratory distress syndrome,
 CC acute lung injury, systemic inflammatory response syndrome (SIRS) and
 CC multiple organ dysfunction (MODS)). The method minimises the pain
 CC and discomfort of injection methods. The present sequence is human

CC mature FLINT protein.
 XX
 SQ Sequence 271 AA.
 Query Match 91.2%; Score 1491; DB 23; Length 271;
 Best Local Similarity 100.0%; Pred. No. 2,7e-110;
 Matches 271; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 30 VAETPTVPMRDAETGERLVCAQCPGPTFVORPCRRDSTPTGCPCPRHYYTOFWNLECR 89
 DB 1 VAETPTVPMRDAETGERLVCAQCPGPTFVORPCRRDSTPTGCPCPRHYYTOFWNLECR 60
 QY 90 YCNVLGGEREBARACHATHNRACRCRTGFFAHAGFCLEHASCPPGAGVIAAGTSPONTQ 149
 DB 61 YCNVLGGEREBARACHATHNRACRCRTGFFAHAGFCLEHASCPPGAGVIAAGTSPONTQ 120
 QY 150 CQCPPTGTFSSASSSSSECCOPHRNCTALGLALNPVGSSSHDTLCTGTFPLSTRVPGAE 209
 DB 121 CQCPPTGTFSSASSSSSECCOPHRNCTALGLALNPVGSSSHDTLCTGTFPLSTRVPGAE 180
 QY 210 ECERAVIDFVAFODISIKRLQRLQALAPBEGMPTPRAGRAALQKLRRLTELLGAD 269
 DB 181 ECERAVIDFVAFODISIKRLQRLQALAPBEGMPTPRAGRAALQKLRRLTELLGAD 240
 QY 270 GALVRLQALRVARMPGLERSVREERFLPVH 300
 DB 241 GALVRLQALRVARMPGLERSVREERFLPVH 271

RESULT 49
 AAB19709
 ID AAB19709 standard; Protein; 271 AA.
 AC AAB19709;
 DT 05-FEB-2001 (first entry)
 XX
 DE Protease-resistant FLINT analogue, R218Q substitution.
 XX
 KM FLINT; FAS ligand inhibitory protein; human; protease resistant;
 KM acute lung injury; acute respiratory distress syndrome;
 KM chronic obstructive pulmonary disease; pulmonary fibrosis;
 KM ulcerative colitis; therapy; organ transplantation; substitution;
 KM mutant; muteln.
 XX
 OS Homo sapiens.
 OS Synthetic.
 FH
 FT Key Location/Qualifiers
 FT Misc-difference 218 /note= "Wild-type Arg substituted by Gln"
 PN WO200058466-A2.
 XX
 PD 05-OCT-2000.
 PD
 PF 20-MAR-2000; 2000WO-US06418.
 XX
 PR 30-MAR-1999; 99US-0126839.
 PR 21-JUN-1999; 99US-0140073.
 PR 04-AUG-1999; 99US-0147071.
 PR 20-OCT-1999; 99US-0160524.
 PR 21-OCT-1999; 99US-0160669.
 PR 20-DEC-1999; 99US-0172744.
 PR 26-JAN-2000; 2000US-0178184.
 XX
 PA (ELIT) LILLY & CO ELI.
 PI Micranovic R, Rathnachalam R, Wlitcher DR;
 XX
 DR WPI: 2000-664925/64.
 XX
 PT Novel protease resistant FAS ligand inhibitory protein analogues

PT resistant to in vivo or in vitro proteolysis at amino acid position 218
PT of the mature protein, useful for treating autoimmune diseases
XX
PS Claim 36; Page -: 100pp; English.
XX
CC Novel human FLINT analogues are resistant to proteolysis at
CC position 218 of the wild-type protein (see AAB19705). The present
CC sequence is a specific example of a protease-resistant FLINT
CC analogue in which the Arg residue at position 218 has been
CC substituted by a Gln residue. The FLINT analogue can be obtained
CC by mutagenesis of template FLINT cDNA (see AAB88730) and expressed
CC in recombinant host cells. It is used to prevent or treat acute
CC lung injury, acute respiratory stress syndrome, ulcerative colitis,
CC chronic obstructive pulmonary disease, and pulmonary fibrosis. It
CC is also used to inhibit T lymphocyte activation, to inhibit
CC ischaemic injury during organ transplantation, and as a component
CC of a liquid medium for infusion and preservation of organs (claimed).
CC Resistance to proteolytic cleavage greatly increases in vivo
CC half-life.
CC Note: The present sequence is not shown in the specification but is
CC derived from the human FLINT mature protein sequence given in
CC the Sequence Listing (see AAB19705).
XX
SQ Sequence 271 AA:
Query Match 91.0%; Score 1487; DB 21; Length 271;
Best Local Similarity 99.6%; Pred. No. 5.5e-110;
Matches 270; Conservative 1; Mismatches 0; Indels 0; Gaps 0;
QY 30 VAEPPTVPMRDAEGERLVCAOCPPGTFVQPCRRDSDPTTCGCPPHRYTQFNNYLERCR 89
DB 1 VAEPPTVPMRDAEGERLVCAOCPPGTFVQPCRRDSDPTTCGCPPHRYTQFNNYLERCR 60
QY YCNVLGGEREEARACHATNRRACRCRTGFFAHAGFCLHNASCPGAGVIAPGTPSONTO 149
DB YCNVLGGEREEARACHATNRRACRCRTGFFAHAGFCLHNASCPGAGVIAPGTPSONTO 120
QY 150 CQCPPEPTFSASSSSSEDCOPPHRNCTALGLALNVPSSSHDTLCTSGTGPPLSTRVGAE 209
DB 121 CQCPPEPTFSASSSSSEDCOPPHRNCTALGLALNVPSSSHDTLCTSGTGPPLSTRVGAE 180
QY 210 ECERAVIDFAFODISIKRLQRLQALAEAPGSGPPRACRAALQTLRRRLTELLGAOD 269
DB 181 ECERAVIDFAFODISIKRLQRLQALAEAPGSGPPRACRAALQTLRRRLTELLGAOD 240
QY 270 GALLVRLQALRVARMGLERSVREPLPVH 300
DB 241 GALLVRLQALRVARMGLERSVREPLPVH 271
RESULT 50
AAE03571
ID AAE03571 standard; Protein; 271 AA.
XX
AC AAE03571;
DT 04-AUG-2001 (first entry)
XX
DE Human mature fas ligand inhibitory protein (FLINT) variant, R218Q.
XX
KM Human: fas ligand inhibitory protein; FLINT; acute lung injury; AIDS;
KM TNFR; tumour necrosis factor receptor protein; ulcerative colitis; AIDS;
KM acute respiratory distress syndrome; pulmonary fibrosis; PF; therapy;
KM chronic obstructive pulmonary disease; COPD; acute lung injury; goitre;
KM rheumatoid arthritis; fibroproliferative lung disease; ischaemia; sepsis;
KM fibrotic lung disease; human immunodeficiency virus; HIV; osteoporosis;
KM chronic renal failure; graft-vs-host disease; cutaneous inflammation;
KM vascular leak syndrome; Helicobacter pylori infection; atherosclerosis;
KM insulin dependent diabetes mellitus (IDDM); inflammatory bowel disease;
KM Crohn's disease; pancreatitis; cancer; autoimmune disease; psoriasis;
KM Down's syndrome; multiple sclerosis; cytostatic; nootropic;
KM neuroprotective; vasotropic; mutant; mutein; variant.
XX

OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 218 /note- "Wild type Arg substituted with Gln"
XX
PN MO200142463-A1.
XX
PD 14-JUN-2001.
XX
XX 29-NOV-2000; 2000WO-US30166.
XX
PF 07-DEC-1999; 99US-0169367.
XX
PR 07-DEC-1999; 99US-0169381.
PR 07-DEC-1999; 99US-0169412.
PR 23-MAR-2000; 2000US-0191430.
XX
PA (EHL) LILLY & CO ELI.
XX
PI Lu J, Miltcher DR;
XX
DR WPI: 2001-381684/40.
XX
XX
PT New FLINT polypeptide for treating and/or preventing acute lung injury,
PT acute respiratory distress syndrome, ulcerative colitis, and
PT graft-versus-host disease, comprises O-linked or N-linked
PT oligosaccharides -
XX
PS Example 1; Page -: 60pp; English.
XX
XX The present sequence is human mature fas ligand inhibitory protein
XX (FLINT) variant, R218Q. FLINT, a homologue of tumour necrosis factor
XX receptor protein (TNFR), binds fas ligand (FasL) and thereby preventing
XX the interaction of FasL with fas. FLINT comprising O-linked or N-linked
XX oligosaccharides is useful for preventing or treating acute lung injury
XX (ALI), acute respiratory distress syndrome (ARDS), ulcerative colitis,
XX chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis (PF),
XX to facilitate organ preservation for transplantation and to inhibit T
XX lymphocyte activation. FLINT is useful for treating and/or preventing
XX diseases such as rheumatoid arthritis, fibroproliferative lung disease,
XX fibrotic lung disease, acute lung injury, human immunodeficiency virus
XX (HIV), ischaemia, brain trauma/injury, chronic renal failure, graft-vs-
XX host disease, cutaneous inflammation, vascular leak syndrome,
XX Helicobacter pylori infection, goitre, atherosclerosis, insulin dependent
XX diabetes mellitus (IDDM), osteoporosis, inflammatory bowel disease,
XX Crohn's disease, sepsis, pancreatitis, cancer, autoimmune disease such as
XX psoriasis, Down's syndrome, and multiple sclerosis.
XX Note: The present sequence is not shown in the specification, but is
XX derived from the mature FLINT sequence shown as SEQ ID NO:1 (AAE03567)
XX in sequence listing of the specification.
XX
SQ Sequence 271 AA:
Query Match 91.0%; Score 1487; DB 22; Length 271;
Best Local Similarity 99.6%; Pred. No. 5.5e-110;
Matches 270; Conservative 1; Mismatches 0; Indels 0; Gaps 0;
QY 30 VAEPPTVPMRDAEGERLVCAOCPPGTFVQPCRRDSDPTTCGCPPHRYTQFNNYLERCR 89
DB 1 VAEPPTVPMRDAEGERLVCAOCPPGTFVQPCRRDSDPTTCGCPPHRYTQFNNYLERCR 60
QY YCNVLGGEREEARACHATNRRACRCRTGFFAHAGFCLHNASCPGAGVIAPGTPSONTO 149
DB YCNVLGGEREEARACHATNRRACRCRTGFFAHAGFCLHNASCPGAGVIAPGTPSONTO 120
QY 150 CQCPPEPTFSASSSSSEDCOPPHRNCTALGLALNVPSSSHDTLCTSGTGPPLSTRVGAE 209
DB 121 CQCPPEPTFSASSSSSEDCOPPHRNCTALGLALNVPSSSHDTLCTSGTGPPLSTRVGAE 180
QY 210 ECERAVIDFAFODISIKRLQRLQALAEAPGSGPPRACRAALQTLRRRLTELLGAOD 269
DB 181 ECERAVIDFAFODISIKRLQRLQALAEAPGSGPPRACRAALQTLRRRLTELLGAOD 240

Query Match 91.0%; Score 1487; DB 23; Length 271;
 Best Local Similarity 99.6%; Pred. No. 5.5e-110;
 Matches 270; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 30 VAETPTYPMDAETGERLVCAOCPPGTFVORPCRRDSPTTCGCPRRHYQFNNYERCR 89
 DB 1 VAETPTYPMDAETGERLVCAOCPPGTFVORPCRRDSPTTCGCPRRHYQFNNYERCR 60
 QY 90 YCNVLCGEREERARACHATNRRACRCRTGFFAHAGFCLHASCPPGAGVIAPTGPSQNTQ 149
 DB 61 YCNVLCGEREERARACHATNRRACRCRTGFFAHAGFCLHASCPPGAGVIAPTGPSQNTQ 120
 QY 150 CQPCPGTFSSASSSSSSQCCPHRNCATLGLALNVPSSSHDTLCTSGTFPLSTRVGA 209
 DB 121 CQPCPGTFSSASSSSSSQCCPHRNCATLGLALNVPSSSHDTLCTSGTFPLSTRVGA 180
 QY 210 ECEBAVIDFAFODISIKRLQRLQALEAPEGMGPTRAGRALQKLRRRLTELLGAOD 269
 DB 181 ECEBAVIDFAFODISIKRLQRLQALEAPEGMGPTRAGRALQKLRRRLTELLGAOD 240
 QY 270 GALLVRLQALRVARMGERSVREPLPVH 300
 DB 241 GALLVRLQALRVARMGERSVREPLPVH 271

RESULT 53
 ID AAE03584 standard; Protein: 271 AA.
 AC AAE03584;
 DT 04-AUG-2001 (first entry)

Human mature fas ligand inhibitory protein (FLINT) variant, R218E.

Human: fas ligand inhibitory protein; FLINT; acute lung injury; ALI;
 TNFR; tumour necrosis factor receptor protein; ulcerative colitis; AADS;
 acute respiratory distress syndrome; pulmonary fibrosis; PF; therapy;
 chronic obstructive pulmonary disease; COPD; acute lung injury; goitre;
 rheumatoid arthritis; fibroproliferative lung disease; ischaemia; sepsis;
 chronic lung disease; human immunodeficiency virus; HIV; osteoporosis;
 chronic renal failure; graft-vs-host disease; cutaneous inflammation;
 vascular leak syndrome; Helicobacter pylori infection; atherosclerosis;
 insulin dependent diabetes mellitus (IDDM); inflammatory bowel disease;
 Crohn's disease; pancreatitis; cancer; autoimmune disease; psoriasis;
 Down's syndrome; multiple sclerosis; cytostatic; nocotropic;
 neuroprotective; vasotropic; mutant; mutein; variant.

OS Homo sapiens.
 OS Synthetic.

Key Location/Qualifiers
 MISC-difference 218 /note= "Wild type Arg substituted with Glu"

W0200142463-A1.

14-JUN-2001.

29-NOV-2000; 2000MO-US30166.

07-DEC-1999; 9905-0169367.

07-DEC-1999; 9905-0169381.

07-DEC-1999; 9905-0169412.

23-MAR-2000; 2000US-0191430.

(ELIL) LILLY & CO ELI.

Lu J, Wlitcher DR;

WPI; 2001-381684/40.

PT New FLINT polypeptide for treating and/or preventing acute lung injury,
 PT acute respiratory distress syndrome, ulcerative colitis, and
 PT graft-versus-host disease, comprises O-linked or N-linked
 PT oligosaccharides -
 PS Disclosure; Page -: 60pp; English.

CC The present sequence is human mature fas ligand inhibitory protein
 CC (FLINT) variant, R218E. FLINT, a homologue of tumour necrosis factor
 CC receptor protein (TNFR), binds fas ligand (FasL) and thereby preventing
 CC the interaction of FasL with fas. FLINT comprising O-linked or N-linked
 CC oligosaccharides is useful for preventing or treating acute lung injury
 CC (ALI), acute respiratory distress syndrome (ARDS), ulcerative colitis,
 CC chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis (PF),
 CC to facilitate organ preservation for transplantation and to inhibit T
 CC lymphocyte activation. FLINT is useful for treating and/or preventing
 CC diseases such as rheumatoid arthritis, fibroproliferative lung disease,
 CC fibrotic lung disease, acute lung injury, human immunodeficiency virus
 CC (HIV), ischaemia, brain trauma/injury, chronic renal failure, graft-vs-
 CC host disease, cutaneous inflammation, vascular leak syndrome,
 CC Helicobacter pylori infection, goitre, atherosclerosis, insulin dependent
 CC diabetes mellitus (IDDM), osteoporosis, inflammatory bowel disease,
 CC Crohn's disease, sepsis, pancreatitis, cancer, autoimmune disease such as
 CC psoriasis, Down's syndrome, and multiple sclerosis.
 CC Note: The present sequence is not shown in the specification, but is
 CC derived from the mature FLINT sequence shown as SEQ ID NO:1 (AAE03567)
 CC in sequence listing of the specification.

SO Sequence 271 AA;

Query Match 90.9%; Score 1486; DB 22; Length 271;
 Best Local Similarity 99.6%; Pred. No. 6.6e-110;
 Matches 270; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 30 VAETPTYPMDAETGERLVCAOCPPGTFVORPCRRDSPTTCGCPRRHYQFNNYERCR 89
 DB 1 VAETPTYPMDAETGERLVCAOCPPGTFVORPCRRDSPTTCGCPRRHYQFNNYERCR 60
 QY 90 YCNVLCGEREERARACHATNRRACRCRTGFFAHAGFCLHASCPPGAGVIAPTGPSQNTQ 149
 DB 61 YCNVLCGEREERARACHATNRRACRCRTGFFAHAGFCLHASCPPGAGVIAPTGPSQNTQ 120
 QY 150 CQPCPGTFSSASSSSSSQCCPHRNCATLGLALNVPSSSHDTLCTSGTFPLSTRVGA 209
 DB 121 CQPCPGTFSSASSSSSSQCCPHRNCATLGLALNVPSSSHDTLCTSGTFPLSTRVGA 180
 QY 210 ECEBAVIDFAFODISIKRLQRLQALEAPEGMGPTRAGRALQKLRRRLTELLGAOD 269
 DB 181 ECEBAVIDFAFODISIKRLQRLQALEAPEGMGPTRAGRALQKLRRRLTELLGAOD 240
 QY 270 GALLVRLQALRVARMGERSVREPLPVH 300
 DB 241 GALLVRLQALRVARMGERSVREPLPVH 271

RESULT 54
 ID AAE14582 standard; Protein: 271 AA.
 AC AAE14582;
 DT 01-JUL-2002 (first entry)

Human protease-resistant mature FLINT analogue (R218E).

FLINT, fas ligand inhibitory protein; pulmonary; lung; apoptosis;
 organ failure; liver; pancreas; inflammatory disease;
 neutrophil; sepsis; acute respiratory distress syndrome;
 acute lung injury; systemic inflammatory response syndrome; SIRS;
 multiple organ dysfunction; MODS; human; protease-resistant;
 mutant; mutein.

OS Homo sapiens.

| OS | Synthetic. | Location/Qualifiers |
|----|---|---------------------|
| XX | Key | Location/Qualifiers |
| XX | Misc-difference 218 | |
| XX | /note= "Wild-type Arg is replaced with Glu" | |
| XX | MO200209668-A2. | |
| XX | 07-FEB-2002. | |
| XX | 20-JUL-2001; 2001WO-US21105. | |
| XX | 02-AUG-2000; 2000US-222476P. | |
| XX | (ELIL) LILLY & CO ELI. | |
| XX | Micanovic R, Wlitcher DR; | |
| XX | WPI: 2002-206149/26. | |
| XX | Administering FLINT (FAS ligand inhibitory protein) or FLINT analog, | |
| XX | useful for treating e.g. sepsis or respiratory distress syndrome, | |
| XX | involves pulmonary administration of a therapeutic amount of the FLINT | |
| XX | or FLINT analog - | |
| XX | Disclosure: Page -; 35pp; English. | |
| XX | The invention relates to a new method of administering FLINT | |
| XX | (FAS ligand inhibitory protein) or FLINT analogue that involves pulmonary | |
| XX | administration of a therapeutic amount of the FLINT or FLINT analogue. | |
| XX | The method enables systemic absorption of FLINT through lungs and | |
| XX | significantly reduces or eliminates the need for administering FLINT by | |
| XX | injection or other routes of administration. The method is useful in | |
| XX | treating disorders related to enhanced apoptosis (e.g. organ failure | |
| XX | in liver, kidneys and pancreas) and inflammatory diseases associated with | |
| XX | neutrophil activation (e.g. sepsis, acute respiratory distress syndrome, | |
| XX | acute lung injury, systemic inflammatory response syndrome (SIRS) and | |
| XX | multiple organ dysfunction (MODS)). The method minimises the pain | |
| XX | and discomfort of injection methods. The present sequence is human | |
| XX | protease-resistant mature FLINT analogue (R218E). | |
| XX | Note: The present sequence is not shown in the specification, but | |
| XX | is derived from the mature FLINT protein sequence (SEQ ID NO:1) shown in | |
| XX | Sequence Listing (AAE14578). | |
| XX | Sequence 271 AA; | |
| XX | Query Match 90.98; Score 1486; DB 23; Length 271; | |
| XX | Best Local Similarity 99.68; Pident. No. 6.6e-110; | |
| XX | Matches 270; Conservative 0; Mismatches 1; Indels 0; Gaps 0; | |
| XX | 30 VAEPTPYWMDRAETGERLVCACQCPGTFVORPCRDSPPTGCPPEPRHYTOPWNYLEPCR 89 | |
| XX | 1 VAEPTPYWMDRAETGERLVCACQCPGTFVORPCRDSPPTGCPPEPRHYTOPWNYLEPCR 60 | |
| XX | 90 YCNVLGGEREEARACHATNHRACRCRTGFFAHAGFCLEHASCPCGACVIAFGTPTSONTO 149 | |
| XX | 61 YCNVLGGEREEARACHATNHRACRCRTGFFAHAGFCLEHASCPCGACVIAFGTPTSONTO 120 | |
| XX | 150 CQCPPEPGTFSASSSSSECCOPHRNCTALGLALNPGSSSHDTLTCTGTFPLSTRVPGAE 209 | |
| XX | 121 CQCPPEPGTFSASSSSSECCOPHRNCTALGLALNPGSSSHDTLTCTGTFPLSTRVPGAE 180 | |
| XX | 210 ECERAVIDFVAFODISIKRLRLLOALEAPGMCPTPAGRAALQTLRRRLTELLGAD 269 | |
| XX | 181 ECERAVIDFVAFODISIKRLRLLOALEAPGMCPTPAGRAALQTLRRRLTELLGAD 240 | |
| XX | 270 GALLVRLLOALRVARMGCLERSVREPLFVH 300 | |
| XX | 241 GALLVRLLOALRVARMGCLERSVREPLFVH 271 | |

| | | |
|----|---|---------------------------------------|
| ID | AAV96599 | standard; Protein: 271 AA. |
| XX | | |
| AC | AAV96599; | |
| XX | | |
| DT | 26-SEP-2000 | (first entry) |
| DE | Human mature FLINT. | |
| XX | | |
| KW | FLINT; osteoprotegerin 3; OPG3; tumour necrosis factor receptor; TNFR; | |
| KW | FasL; LIGHT; apoptosis; pro-inflammatory; hepatotropic; vasotropic; | |
| KW | anti-diabetic; anti-anemic; neuroprotective; anti-ulcer; cyostatic; | |
| KW | anti-inflammatory; antibacterial; immunosuppressive. | |
| OS | Homo sapiens. | |
| XX | | |
| PN | WO200037094-A2. | |
| PD | 29-JUN-2000. | |
| XX | | |
| PF | 21-DEC-1999; 99WO-US30734. | |
| XX | | |
| XX | 22-DEC-1998; 98US-0133407. | |
| PR | 30-MAR-1999; 99WO-US06797. | |
| PR | 20-OCT-1999; 99US-0172239. | |
| XX | | |
| PA | (ELIL) LILLY & CO ELI. | |
| XX | | |
| PI | Cohen FJ, Posada JA, Wierda D; | |
| XX | | |
| DR | WPI: 2000-475441/41. | |
| DR | N-PSDB: AAA51078. | |
| XX | | |
| PT | Use of mature FLINT for treating e.g. acute respiratory distress | |
| PT | syndrome, ulcerative colitis or ischemic injury during organ | |
| PT | transplantation | |
| XX | | |
| PS | Example 1; Fig 4A-B; 125pp; English. | |
| XX | | |
| CC | Human FLINT (also known as osteoprotegerin 3) is a new tumour necrosis | |
| CC | factor receptor (TNFR) superfamily member, which binds FasL and LIGHT and | |
| CC | prevents FasL-Fas interaction. Mature FLINT (mFLINT) inhibits FasL-Fas | |
| CC | mediated apoptotic and pro-inflammatory activity. mFLINT is useful for | |
| CC | treating acute respiratory distress syndrome, treating or inhibiting | |
| CC | ulcerative colitis, inhibiting ischemic injury during organ | |
| CC | transplantation or for organ preservation during transplantation. mFLINT | |
| CC | can also be used to treat acute liver failure, inflammation of the liver, | |
| CC | abnormal (hepatocyte) apoptosis, sepsis, disorders associated with | |
| CC | inflammation, hepatitis, ischemia, hypercoagulation or reperfusion, | |
| CC | damage to a cardiac myocyte resulting from abnormal myocardial ischemia, | |
| CC | Type I diabetes, cancer, damage to an innocent bystander tissue induced | |
| CC | by a chemotherapeutic or therapeutic irradiation, aplastic anaemias, | |
| CC | myelodysplastic syndromes and pancytopenic conditions. | |
| XX | | |
| XX | Sequence 271 AA; | |
| XX | | |
| QY | Query Match | 90.9%; Score 1485; DB 21; Length 271; |
| Db | Best Local Similarity | 99.6%; Pred. No. 8e-110; |
| | Matches 270; Conservative | 0; Mismatches 1; Indels 0; Gaps 0; |
| QY | 30 VAEPTPYVWRDAETGERLVCAQCPGTFVQRPCCRRDSEPTTCGCPPRHYTQFMWYLERCR | 89 |
| Db | 1 VAEPTPYVWRDAETGERLVCAQCPGTFVQRPCCRRDSEPTTCGCPPRHYTQFMWYLERCR | 60 |
| QY | 90 YCNVLGGEREAEAAACHATNHRACRCRGRFAAHAGFCLAEHASCPPGAGVITAPGPSQNTQ | 149 |
| Db | 61 YCNVLGGEREAEAAACHATNHRACRCRGRFAAHAGFCLAEHASCPPGAGVITAPGPSQNTQ | 120 |
| QY | 150 CQCPPEPTGFSASSSSSEOCOPHRMCTALGALANTPGSSSHPTLTCTSGTGFPLSTRVPAAE | 209 |
| Db | 121 CQCPPEPTGFSASSSSSEOCOPHRMCTALGALANTPGSSSHPTLTCTSGTGFPLSTRVPAAE | 180 |
| QY | 210 ECEAAVDAIFAAODISIKRLQRLQALAEAPGWCPTPRAGAAQLQLARRLTLLGAQD | 269 |

CC injection or other routes of administration. The method is useful in
 CC treating disorders related to enhanced apoptosis (e.g. organ failure
 CC in liver, kidneys and pancreas) and inflammatory diseases associated with
 CC neutrophil activation (e.g. sepsis, acute respiratory distress syndrome,
 CC acute lung injury, systemic inflammatory response syndrome (SIRS) and
 CC multiple organ dysfunction (MODS)). The method minimises the pain
 CC and discomfort of injection methods. The present sequence is human
 CC protease-resistant mature FLINT analogue (R218S).
 CC Note: The present sequence is not shown in the specification, but
 CC is derived from the mature FLINT protein sequence (SEQ ID NO:1) shown in
 CC Sequence Listing (AAE14578).

XX Sequence 271 AA;

Query Match 90.9%; Score 1485; DB 23; Length 271;
 Best Local Similarity 99.6%; Pred. No. 8e-110;
 Matches 270; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

OY 30 VAETPTVWMDAETGERLVCAQCPGTFVQRPGRDSTPTGCPPRHYTOFWMYLERCR 89
 DB 1 VAETPTVWMDAETGERLVCAQCPGTFVQRPGRDSTPTGCPPRHYTOFWMYLERCR 60
 OY 90 YCNVLCGEREEBARACHATNRACRCRTGFFAHAGFCLEHASCPGACVIAAGPSPONTQ 149
 DB 61 YCNVLCGEREEBARACHATNRACRCRTGFFAHAGFCLEHASCPGACVIAAGPSPONTQ 120
 OY 150 CQPCPGTFSSASSSSSECOFHRNCTALGLALNPGSSSHDTLCSTGFPPLSTVPPAE 209
 DB 121 CQPCPGTFSSASSSSSECOFHRNCTALGLALNPGSSSHDTLCSTGFPPLSTVPPAE 180
 OY 210 ECERAVIDFAFODISIKRLQRLQALBAPGCGPTPAGRAAQLKLRRLTTELLGAOD 269
 DB 181 ECERAVIDFAFODISIKRLQRLQALBAPGCGPTPAGRAAQLKLRRLTTELLGAOD 240
 OY 270 GALLVRLQLALRVARMPLERSVRRFLPVH 300
 DB 241 GALLVRLQLALRVARMPLERSVRRFLPVH 271

RESULT 58

ID AAE14586 standard; Protein: 271 AA.

XX AAE14586;

DT 01-JUL-2002 (first entry)

DE Human protease-resistant mature FLINT analogue (R218S).

XX FLINT; FAS ligand inhibitory protein; pulmonary; lung; apoptosis;
 KW organ failure; liver; kidney; pancreas; inflammatory disease;
 KW neutrophil; sepsis; acute respiratory distress syndrome;
 KW acute lung injury; systemic inflammatory response syndrome; SIRS;
 KW multiple organ dysfunction; MODS; human; protease-resistant;
 KW mutant; mutein.

XX Homo sapiens.
 OS Synthetic.

XX Key Location/Qualifiers
 FH Misc-difference 218 /note= "Wild-type Arg is replaced with Ser"
 FT
 XX

PM WO200209668-A2.

XX 07-FEB-2002.

XX 20-JUL-2001; 2001WO-US21105.

XX 02-AUG-2000; 2000US-222476P.

XX (ELIL) LILLY & CO ELI.

PI Micanovic R, Wlitcher DR;

XX WPI: 2002-206149/26.

PT Administering FLINT (FAS ligand inhibitory protein) or FLINT analog,
 PT useful for treating e.g. sepsis or respiratory distress syndrome,
 PT involves pulmonary administration of a therapeutic amount of the FLINT
 PT or FLINT analog -
 XX Disclosure: Page -; 35pp; English.

XX The invention relates to a new method of administering FLINT
 CC (FAS ligand inhibitory protein) or FLINT analogue that involves pulmonary
 CC administration of a therapeutic amount of the FLINT or FLINT analogue.

CC The method enables systemic absorption of FLINT through lungs and
 CC significantly reduces or eliminates the need for administering FLINT by
 CC injection or other routes of administration. The method is useful in
 CC treating disorders related to enhanced apoptosis (e.g. organ failure
 CC in liver, kidneys and pancreas) and inflammatory diseases associated with
 CC neutrophil activation (e.g. sepsis, acute respiratory distress syndrome,
 CC acute lung injury, systemic inflammatory response syndrome (SIRS) and
 CC multiple organ dysfunction (MODS)). The method minimises the pain
 CC and discomfort of injection methods. The present sequence is human
 CC protease-resistant mature FLINT analogue (R218S).

CC Note: The present sequence is not shown in the specification, but
 CC is derived from the mature FLINT protein sequence (SEQ ID NO:1) shown in
 CC Sequence Listing (AAE14578).

XX Sequence 271 AA;

Query Match 90.9%; Score 1485; DB 23; Length 271;
 Best Local Similarity 99.6%; Pred. No. 8e-110;
 Matches 270; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

OY 30 VAETPTVWMDAETGERLVCAQCPGTFVQRPGRDSTPTGCPPRHYTOFWMYLERCR 89
 DB 1 VAETPTVWMDAETGERLVCAQCPGTFVQRPGRDSTPTGCPPRHYTOFWMYLERCR 60
 OY 90 YCNVLCGEREEBARACHATNRACRCRTGFFAHAGFCLEHASCPGACVIAAGPSPONTQ 149
 DB 61 YCNVLCGEREEBARACHATNRACRCRTGFFAHAGFCLEHASCPGACVIAAGPSPONTQ 120
 OY 150 CQPCPGTFSSASSSSSECOFHRNCTALGLALNPGSSSHDTLCSTGFPPLSTVPPAE 209
 DB 121 CQPCPGTFSSASSSSSECOFHRNCTALGLALNPGSSSHDTLCSTGFPPLSTVPPAE 180
 OY 210 ECERAVIDFAFODISIKRLQRLQALBAPGCGPTPAGRAAQLKLRRLTTELLGAOD 269
 DB 181 ECERAVIDFAFODISIKRLQRLQALBAPGCGPTPAGRAAQLKLRRLTTELLGAOD 240
 OY 270 GALLVRLQLALRVARMPLERSVRRFLPVH 300
 DB 241 GALLVRLQLALRVARMPLERSVRRFLPVH 271

RESULT 59

ID AAE14590 standard; Protein: 271 AA.

XX AAE14590;

DT 01-JUL-2002 (first entry)

DE Human protease-resistant mature FLINT analogue (T216P).

XX FLINT; FAS ligand inhibitory protein; pulmonary; lung; apoptosis;
 KW organ failure; liver; kidney; pancreas; inflammatory disease;
 KW neutrophil; sepsis; acute respiratory distress syndrome;
 KW acute lung injury; systemic inflammatory response syndrome; SIRS;
 KW multiple organ dysfunction; MODS; human; protease-resistant;
 KW mutant; mutein.

XX Homo sapiens.

OS Synthetic. Location/Qualifiers
XX Key
FH Misc-difference 216
FT /note= "Wild-type Thr is replaced with Pro"
XX
XX PN WO200209668-A2.
XX
XX PD 07-FEB-2002.
XX PF 20-JUL-2001; 2001WO-US21105.
XX PR 02-AUG-2000; 2000US-222476P.
XX PA (ELIL) LILLY & CO ELI.
XX PI Micanovic R, Wlitcher DR;
XX DR WPI: 2002-206149/26.
XX
XX Administering FLINT (FAS ligand inhibitory protein) or FLINT analog,
PT useful for treating e.g. sepsis or respiratory distress syndrome,
PT involves pulmonary administration of a therapeutic amount of the FLINT
or FLINT analog -
XX
XX PS Disclosure: Page -: 35pp; English.
XX
XX CC The invention relates to a new method of administering FLINT
CC (FAS ligand inhibitory protein) or FLINT analogue that involves pulmonary
CC administration of a therapeutic amount of the FLINT or FLINT analogue.
CC The method enables systemic absorption of FLINT through lungs and
CC significantly reduces or eliminates the need for administering FLINT by
CC injection or other routes of administration. The method is useful in
CC treating disorders related to enhanced apoptosis (e.g. organ failure
CC in liver, kidneys and pancreas) and inflammatory diseases associated with
CC neutrophil activation (e.g. sepsis, acute respiratory distress syndrome,
CC acute lung injury, systemic inflammatory response syndrome (SIRS) and
CC multiple organ dysfunction (MODS)). The method minimises the pain
CC and discomfort of injection methods. The present sequence is human
CC protease-resistant mature FLINT analogue (R218G).
CC Note: The present sequence is not shown in the specification, but
CC is derived from the mature FLINT protein sequence (SEQ ID NO:1) shown in
CC Sequence Listing (AAE14578).
XX
XX SO Sequence 271 AA:
SQ
Query Match 90.9%; Score 1485; DB 23; Length 271;
Best Local Similarity 99.6%; Pred. No. 8e-110;
Matches 270; Conservative 0; Mismatches 1; Indels 0; Gaps 0;
OY 30 VAETPTYPWDAETGERLVCAQCPPTGVORPCRRDSPTTCGCPPRHHTQFMWNYLERCR 89
DB 1 VAETPTYPWDAETGERLVCAQCPPTGVORPCRRDSPTTCGCPPRHHTQFMWNYLERCR 60
OY YCNVLCGEREEBARACHATNRRACRCRTGFFAHAGFLEHASCPPGAGVIAPGTPSONTO 149
DB 61 YCNVLCGEREEBARACHATNRRACRCRTGFFAHAGFLEHASCPPGAGVIAPGTPSONTO 120
OY 150 CQCPPTGTFSSASSSSSECCQPHRNCTALGALNVPSSSHDTLCTSCGFFPLSTRVPAE 209
DB 121 CQCPPTGTFSSASSSSSECCQPHRNCTALGALNVPSSSHDTLCTSCGFFPLSTRVPAE 180
OY 210 ECEBRAVIDEVAFODISIKRIQLQALEAPRGWGPPTPRAGRAALQKLRRRLTELGAD 269
DB 181 ECEBRAVIDEVAFODISIKRIQLQALEAPRGWGPPTPRAGRAALQKLRRRLTELGAD 240
OY 270 GALLVRLQLALRVARMGRLERSVVERPLPVH 300
DB 241 GALLVRLQLALRVARMGRLERSVVERPLPVH 271

ID AAE14585 standard; Protein: 271 AA.
XX
XX AAE14585;
XX
XX 01-JUL-2002 (first entry)
XX
XX Human protease-resistant mature FLINT analogue (R218G).
XX
XX FLINT; FAS ligand inhibitory protein; pulmonary; lung; apoptosis;
XX organ failure; liver; kidney; pancreas; inflammatory disease;
XX neutrophil; sepsis; acute respiratory distress syndrome;
XX acute lung injury; systemic inflammatory response syndrome; SIRS;
XX multiple organ dysfunction; MODS; human; protease-resistant;
XX mutant; mulein.
XX
XX OS Homo sapiens.
XX OS Synthetic.
XX
XX FH Key Location/Qualifiers
FH Misc-difference 218
FT /note= "Wild-type Arg is replaced with Gly"
XX
XX PN WO200209668-A2.
XX
XX PD 07-FEB-2002.
XX PF 20-JUL-2001; 2001WO-US21105.
XX PR 02-AUG-2000; 2000US-222476P.
XX PA (ELIL) LILLY & CO ELI.
XX PI Micanovic R, Wlitcher DR;
XX DR WPI: 2002-206149/26.
XX
XX Administering FLINT (FAS ligand inhibitory protein) or FLINT analog,
PT useful for treating e.g. sepsis or respiratory distress syndrome,
PT involves pulmonary administration of a therapeutic amount of the FLINT
or FLINT analog -
XX
XX PS Disclosure: Page -: 35pp; English.
XX
XX CC The invention relates to a new method of administering FLINT
XX (FAS ligand inhibitory protein) or FLINT analogue that involves pulmonary
XX administration of a therapeutic amount of the FLINT or FLINT analogue.
XX The method enables systemic absorption of FLINT through lungs and
XX significantly reduces or eliminates the need for administering FLINT by
XX injection or other routes of administration. The method is useful in
XX treating disorders related to enhanced apoptosis (e.g. organ failure
XX in liver, kidneys and pancreas) and inflammatory diseases associated with
XX neutrophil activation (e.g. sepsis, acute respiratory distress syndrome,
XX acute lung injury, systemic inflammatory response syndrome (SIRS) and
XX multiple organ dysfunction (MODS)). The method minimises the pain
XX and discomfort of injection methods. The present sequence is human
XX protease-resistant mature FLINT analogue (R218G).
XX Note: The present sequence is not shown in the specification, but
XX is derived from the mature FLINT protein sequence (SEQ ID NO:1) shown in
XX Sequence Listing (AAE14578).
XX
XX SO Sequence 271 AA:
SQ
Query Match 90.8%; Score 1484; DB 23; Length 271;
Best Local Similarity 99.6%; Pred. No. 9.6e-110;
Matches 270; Conservative 0; Mismatches 1; Indels 0; Gaps 0;
OY 30 VAETPTYPWDAETGERLVCAQCPPTGVORPCRRDSPTTCGCPPRHHTQFMWNYLERCR 89
DB 1 VAETPTYPWDAETGERLVCAQCPPTGVORPCRRDSPTTCGCPPRHHTQFMWNYLERCR 60
OY YCNVLCGEREEBARACHATNRRACRCRTGFFAHAGFLEHASCPPGAGVIAPGTPSONTO 149
DB 61 YCNVLCGEREEBARACHATNRRACRCRTGFFAHAGFLEHASCPPGAGVIAPGTPSONTO 120

| | | | |
|-----------|---|---|-----|
| QY | 150 | CCPCPCPGCTSSASSSSSECCQCPHNRCTALGALINPVGSSSHDTLTCTGCPPLSTRPGAE | 209 |
| Db | 121 | CCPCPCPGCTSSASSSSSECCQCPHNRCTALGALINPVGSSSHDTLTCTGCPPLSTRPGAE | 180 |
| QY | 210 | ECERAVIDVAFODISIKRLORLQALAPAGGWPPTPAGRAALQKLRRRLTEILGAOD | 269 |
| Db | 181 | ECERAVIDVAFODISIKRLORLQALAPAGGWPPTPAGRAALQKLRRRLTEILGAOD | 240 |
| QY | 270 | GALLVRLQLALRVARMPGLERSVREPLDPVH | 300 |
| Db | 241 | GALLVRLQLALRVARMPGLERSVREPLDPVH | 271 |
| RESULT 61 | | | |
| ID | AAEL14588 | standard; Protein; 271 AA. | |
| AC | AAEL14588 | | |
| XX | | | |
| DT | 01-JUL-2002 | (first entry) | |
| DE | | Human protease-resistant mature FLINT analogue (R218Y). | |
| XX | | | |
| KW | FLINT; FAS ligand inhibitory protein; pulmonary; lung; apoptosis; | | |
| KW | organ failure; liver; kidney; pancreas; inflammatory disease; | | |
| KW | neutrophil; sepsis; acute respiratory distress syndrome; | | |
| KW | acute lung injury; systemic inflammatory response syndrome; SIRS; | | |
| KW | multiple organ dysfunction; MODS; human; protease-resistant; | | |
| KW | mutant; mutein. | | |
| OS | Homo sapiens. | | |
| OS | Synthetic. | | |
| XX | | | |
| PH | Key | Location/Qualifiers | |
| FT | Misc-difference | 218 | |
| FT | /note= "Wild-type Arg is replaced with Tyr" | | |
| PN | WO200209668-A2. | | |
| PD | 07-FEB-2002. | | |
| XX | | | |
| PF | 20-JUL-2001; 2001WO-US21105. | | |
| PR | 02-AUG-2000; 2000US-222476P. | | |
| XX | | | |
| PA | (ELIL) LILLY & CO ELI. | | |
| PI | Micanovic R, Witcher DR. | | |
| DR | WPI; 2002-206149/26. | | |
| XX | | | |
| PT | Administering FLINT (FAS ligand inhibitory protein) or FLINT analog, | | |
| PT | useful for treating e.g. sepsis or respiratory distress syndrome, | | |
| PT | involves pulmonary administration of a therapeutic amount of the FLINT | | |
| XX | or FLINT analog - | | |
| PS | Disclosure; Page -: 35pp; English. | | |
| CC | The invention relates to a new method of administering FLINT | | |
| CC | (FAS ligand inhibitory protein) or FLINT analogue that involves pulmonary | | |
| CC | administration of a therapeutic amount of the FLINT or FLINT analogue. | | |
| CC | The method enables systemic absorption of FLINT through lungs and | | |
| CC | significantly reduces or eliminates the need for administering FLINT by | | |
| CC | injection or other routes of administration. The method is useful in | | |
| CC | treating disorders related to enhanced apoptosis (e.g. organ failure | | |
| CC | in liver, kidneys and pancreas) and inflammatory diseases associated with | | |
| CC | neutrophil activation (e.g. sepsis, acute respiratory distress syndrome, | | |
| CC | acute lung injury, systemic inflammatory response syndrome (SIRS) and | | |
| CC | multiple organ dysfunction (MODS)). The method minimises the pain | | |
| CC | and discomfort of injection methods. The present sequence is human | | |
| CC | protease-resistant mature FLINT analogue (R218Y). | | |
| CC | Note: The present sequence is not shown in the specification, but | | |

| | | |
|-----------|--|--|
| CC | | is derived from the mature FLINT protein sequence (SEQ ID NO:1) shown in |
| CC | Sequence Listing (AAE14578). | |
| XX | | |
| SQ | Sequence 271 AA; | |
| | | |
| | Query Match | 90.8%; Score 1484; DB 23; Length 271; |
| | Best Local Similarity | 99.6%; Pred. No.9.6e-110; |
| | Matches 270; Conservative | 0; Mismatches 1; Indels 0; Gaps 0; |
| OY | 30 VAETPTVWRAAEGERLVCACCPGTFVORPCRRDSPTCGPCPPRHHTYOFMWYLESCR | 89 |
| Dd | | |
| OY | 1 VAEPTTYWRAAEGERLVCACCPGTFVQRCRDSFTTGGPCPPRIHYTOFWMYLESCR | 60 |
| Dd | | |
| OY | 90 YCNVLGGEREEBARCAHATHNRACRCRTGFPAHAGFCLENASCPGAGVIAPGTPSQNTQ | 149 |
| Dd | | |
| OY | 61 YCNVLGGEREEBARCAHATHNRACRCRTGFPAHAGFCLENASCPGAGVIAPGTPSQNTQ | 120 |
| OY | 150 CQCPPEGTFSASSSSSECCQHNCNTAIGLALNPGSSSHDTLTCTSCGFPILSTRVPAAE | 209 |
| Dd | | |
| OY | 121 CQCPPEGTFSASSSSSECCQHNCNTAIGLALNPGSSSHDTLTCTSCGFPILSTRVPAAE | 180 |
| OY | 210 ECEARAVIDFAFODISIKRLQRLQALAPAGWGPTPAGRAALQKLRRRLTELLGAOD | 269 |
| Dd | | |
| OY | 181 ECEARAVIDFAFODISIKRLQRLQALAPAGWGPTPAGRAALQKLRRRLTELLGAOD | 240 |
| Dd | | |
| OY | 270 GALLVRLLQALRVARMPGLERSVRERLFVH 300 | |
| Dd | | |
| | 241 GALLVRLLQALRVARMPGLERSVRERLFVH 271 | |
| | | |
| RESULT 62 | | |
| ID | AAE14587 | |
| ID | AAE14587 standard; Protein; 271 AA. | |
| XX | | |
| AC | AAE14587; | |
| DX | | |
| DT | 01-JUL-2002 (first entry) | |
| XX | | |
| DE | Human protease-resistant mature FLINT analogue (R218V). | |
| XX | | |
| KW | FLINT; FAS ligand inhibitory protein; pulmonary; lung; apoptosis; | |
| KW | organ failure; liver; kidney; pancreas; inflammatory disease; | |
| KW | neutrophil; sepsis; acute respiratory distress syndrome; | |
| KW | acute lung injury; systemic inflammatory response syndrome; SIRS; | |
| KW | multiple organ dysfunction; MODS; human; protease-resistant; | |
| KW | mutant; mutlein. | |
| XX | | |
| OS | Homo sapiens. | |
| OS | Synthetic. | |
| XX | | |
| FH | Key Location/Qualifiers | |
| FT | Misc-difference 218 /note= "Wild-type Arg is replaced with Val" | |
| XX | | |
| PN | WO200209668-A2. | |
| XX | | |
| PD | 07-FEB-2002. | |
| XX | | |
| PF | 20-JUL-2001; 2001WO-US21105. | |
| XX | | |
| PR | 02-AUG-2000; 2000US-222476P. | |
| XX | | |
| PA | (ELIL) LILLY & CO ELI. | |
| XX | | |
| PI | Micanovic R, Witcher DR; | |
| XX | | |
| DR | WPI; 2002-206149/26. | |
| XX | | |
| PT | Administering FLINT (FAS ligand inhibitory protein) or FLINT analog, | |
| PT | useful for treating e.g. sepsis or respiratory distress syndrome, | |
| PT | involves pulmonary administration of a therapeutic amount of the FLINT | |
| XX | or FLINT analog - | |
| XX | | |

XX AAE14589;
AC
XX 01-JUL-2002 (first entry)
DE Human protease-resistant mature FLINT analogue (P217Y).
XX
XX FLINT; FAS ligand inhibitory protein; pulmonary; lung; apoptosis;
KW organ failure; liver; kidney; pancreas; inflammatory disease;
KW neutrophil; sepsis; acute respiratory distress syndrome;
KW acute lung injury; systemic inflammatory response syndrome; SIRS;
KW multiple organ dysfunction; MODS; human; protease-resistant;
KW mutant; muten.
XX
XX Homo sapiens.
OS Synthetic.
XX
XX Key Location/Qualifiers
FH Misc-difference 217
FT /note= "Wild-type Pro is replaced with Tyr"
FT
XX WO200209668-A2.
XX
XX 07-FEB-2002.
XX
XX 20-JUL-2001; 2001WO-US21105.
XX
XX 02-AUG-2000; 2000US-222476P.
XX
XX (ELIL) LILLY & CO ELI.
XX
XX Micanovic R, Witcher DR;
XX
XX WPI: 2002-206149/26.
XX
XX Administering FLINT (FAS ligand inhibitory protein) or FLINT analog,
PT useful for treating e.g. sepsis or respiratory distress syndrome,
PT involves pulmonary administration of a therapeutic amount of the FLINT
PT or FLINT analog -
XX
XX Disclosure: Page -, 35pp; English.
XX
XX The invention relates to a new method of administering FLINT
CC (FAS ligand inhibitory protein) or FLINT analogue that involves pulmonary
CC administration of a therapeutic amount of the FLINT or FLINT analogue.
CC The method enables systemic absorption of FLINT through lungs and
CC significantly reduces or eliminates the need for administering FLINT by
CC injection or other routes of administration. The method is useful in
CC treating disorders related to enhanced apoptosis (e.g. organ failure
CC in liver, kidneys and pancreas) and inflammatory diseases associated with
CC neutrophil activation (e.g. sepsis, acute respiratory distress syndrome,
CC acute lung injury, systemic inflammatory response syndrome (SIRS) and
CC multiple organ dysfunction (MODS)). The method minimizes the pain
CC and discomfort of injection methods. The present sequence is human
CC protease-resistant mature FLINT analogue (P217Y).
CC Note: The present sequence is not shown in the specification, but
CC is derived from the mature FLINT protein sequence (SEQ ID NO:1) shown in
CC Sequence listing (AAE14578).
XX
XX
SQ Sequence 271 AA;
Query Match 90.6%; Score 1481; DB 23; Length 271;
Best Local Similarity 99.6%; Pred. No. 1.7e-109;
Matches 270; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 150 CQPCPGTFFSASSSSSEOCOPHRNCTALGLANVPSSSHDTLCTSGTFLSTRVPGAE 209
AC
XX
DB 121 CQPCPGTFFSASSSSSEOCOPHRNCTALGLANVPSSSHDTLCTSGTFLSTRVPGAE 180
QY 210 ECERAVIDEVAFQDISIKRLQALQALEAPGSGPTPAGRAALQKLRRRLTELLGAOD 269
DB 181 ECERAVIDEVAFQDISIKRLQALQALEAPGSGPTPAGRAALQKLRRRLTELLGAOD 240
QY 270 GALLVRLQALRVARMGLESVDERPLPVH 300
DB 241 GALLVRLQALRVARMGLESVDERPLPVH 271
RESULT 65
AAB19706
ID AAB19706 standard; Protein: 271 AA.
AC
XX AAB19706;
XX
XX 05-FEB-2001 (first entry)
DE
XX
XX Protease-resistant FLINT analogue, R34N, D36T, R218Q substitution.
DE
XX
XX FLINT; FAS ligand inhibitory protein; human; protease resistant;
KW acute lung injury; acute respiratory distress syndrome;
KW chronic obstructive pulmonary disease; pulmonary fibrosis;
KW ulcerative colitis; therapy; organ transplantation; substitution;
KW mutant; muten.
XX
XX Homo sapiens.
OS Synthetic.
XX
XX
XX Key Location/Qualifiers
FH Misc-difference 34
FT /note= "Wild-type Arg substituted by Asn"
FT Misc-difference 36
FT /note= "Wild-type Asp substituted by Thr"
FT Misc-difference 218
FT /note= "Wild-type Arg substituted by Gln"
XX
XX WO200058466-A2.
XX
XX
XX 05-OCT-2000.
XX
XX 20-MAR-2000; 2000WO-US06418.
XX
XX 30-MAR-1999; 99US-0126839.
XX 21-JUN-1999; 99US-0140073.
XX 04-AUG-1999; 99US-0147071.
XX 20-OCT-1999; 99US-0160524.
XX 21-OCT-1999; 99US-0160669.
XX 20-DEC-1999; 99US-0172744.
XX 26-JAN-2000; 2000US-0178184.
XX
XX (ELIL) LILLY & CO ELI.
XX
XX Micanovic R, Rathnachalam R, Witcher DR;
XX
XX WPI: 2000-664925/64.
XX
XX Novel protease resistant FAS ligand inhibitory protein analogues
PT resistant to in vivo or in vitro proteolysis at amino acid position 218
PT of the mature protein, useful for treating autoimmune diseases -
XX
XX Claim 13; Page -, 100pp; English.
XX
XX Novel human FLINT analogues are resistant to proteolysis at
CC position 218 of the wild-type protein (see AAB19705). The present
CC sequence is a specific example of a protease-resistant FLINT
CC analogue in which the Arg residue at position 34 has been
CC substituted by an Asn residue, the Asp residue at position 36 has
CC been substituted by a Thr residue, and the Arg residue at position
CC 218 has been substituted by a Gln residue. The FLINT analogue can

CC be obtained by mutagenesis of template FLINT cDNA (see AAA8730) and
 CC expressed in recombinant host cells. It is used to prevent or
 CC treat acute lung injury, acute respiratory stress syndrome,
 CC ulcerative colitis, chronic obstructive pulmonary disease, and
 CC pulmonary fibrosis. It is also used to inhibit T lymphocyte
 CC activation, to inhibit ischemic injury during organ
 CC transplantation, and as a component of a liquid medium for
 CC infusion and preservation of organs (claimed). Resistance to
 CC proteolytic cleavage greatly increases in vivo half-life.
 CC Note: The present sequence is not shown in the specification but is
 CC derived from the human FLINT mature protein sequence given in
 CC the Sequence Listing (see AAB19705).

XX SQ Sequence 271 AA:

Query Match 90.3%; Score 1475; DB 21; Length 271;
 Best Local Similarity 98.9%; Pred. No. 4.9e-109;
 Matches 268; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

QY 30 VAETPTVPMRDAETGERLVCAOCPPGTFVORPCRDSPPTGCPGPPRHYYQFMNLYERCR 89
 DB 1 VAETPTVPMRDAETGERLVCAOCPPGTFVORPCRDSPPTGCPGPPRHYYQFMNLYERCR 60
 QY YCNVLCGEREEBAAACHATNHRACRCRTGFFAHAGFCLHASCPPGAGVIAPGTPSONTQ 149
 DB 61 YCNVLCGEREEBAAACHATNHRACRCRTGFFAHAGFCLHASCPPGAGVIAPGTPSONTQ 120
 QY 150 CQPCPGTFSSASSSSSQCPHNRCTALGLALNVPSSSDTLCTSCGFPPLSTRVPGA 209
 DB 121 CQPCPGTFSSASSSSSQCPHNRCTALGLALNVPSSSDTLCTSCGFPPLSTRVPGA 180
 QY 210 ECERAVIDFAFODISIKRLQRLQALEAPGCGPTPRAGRAALQKLRRRLTELLGAOD 269
 DB 181 ECERAVIDFAFODISIKRLQRLQALEAPGCGPTPRAGRAALQKLRRRLTELLGAOD 240
 QY 270 GALLVRLQALRVARMGELERSVREPLPVH 300
 DB 241 GALLVRLQALRVARMGELERSVREPLPVH 271

RESULT 66

ID AAB68046 standard; Protein: 271 AA.

AC AAB68046;

DT 29-JUN-2001 (first entry)

DE Amino acid sequence of a modified human mature FLINT polypeptide.

XX FLINT; FAS ligand inhibitory protein; divalent metal cation; Fas;
 KW Fas ligand; acute liver failure; cerebral ischemia; apoptosis.

XX Homo sapiens.

XX Key Location/Qualifiers

FT MISC-difference 34 /note= "Arg replaced by Asn"

FT MISC-difference 36 /note= "Asp replaced by Thr"

FT MISC-difference 194 /note= "Asp replaced by Asn"

FT MISC-difference 196 /note= "Ser replaced by Thr"

XX WO200118055-A1.

XX 15-MAR-2001.

XX 31-AUG-2000; 2000WO-US20807.

XX 10-SEP-1999; 99US-0153339.

PA (ELIL) LILLY & CO ELI.

XX Atkinson PR, Tian Y, Witcher DR;

XX WPI: 2001-273382/28.

XX Compositions comprising a divalent metal cation and a FAS ligand
 PT Inhibitory Protein (FLINT), for reducing or inducing aggregation of
 PT FLINT and for treating diseases involving Fas/Fas and/or
 PT LIGHT/LT-beta-R receptor interactions
 XX Example 1; Page -: 44pp; English.

XX The present sequence represents a modified mature FLINT (FAS ligand
 CC Inhibitory Protein) polypeptide. The specification describes a
 CC composition comprising a divalent metal cation and FLINT protein. The
 CC composition is used either for reducing, reversing or eliminating
 CC aggregation and precipitation of FLINT or for inducing oligomerisation
 CC or aggregation of FLINT molecules. They can be used for purifying FLINT
 CC and/or maintaining FLINT in solution. The compositions are used to treat
 CC and/or prevent disorders associated with the binding of Fas to FasL
 CC and/or LIGHT to the lmpetar and/or TR2/HVEM receptors. Uses include the
 CC treatment of acute liver failure and cerebral ischemia and the prevention
 CC of apoptosis.
 CC note: this sequence does not appear in the specification; it was created
 CC using information provided.

XX SQ Sequence 271 AA:

Query Match 90.0%; Score 1471; DB 22; Length 271;
 Best Local Similarity 96.3%; Pred. No. 1e-108;
 Matches 267; Conservative 2; Mismatches 2; Indels 0; Gaps 0;

QY 30 VAETPTVPMRDAETGERLVCAOCPPGTFVORPCRDSPPTGCPGPPRHYYQFMNLYERCR 89
 DB 1 VAETPTVPMRDAETGERLVCAOCPPGTFVORPCRDSPPTGCPGPPRHYYQFMNLYERCR 60
 QY YCNVLCGEREEBAAACHATNHRACRCRTGFFAHAGFCLHASCPPGAGVIAPGTPSONTQ 149
 DB 61 YCNVLCGEREEBAAACHATNHRACRCRTGFFAHAGFCLHASCPPGAGVIAPGTPSONTQ 120
 QY 150 CQPCPGTFSSASSSSSQCPHNRCTALGLALNVPSSSDTLCTSCGFPPLSTRVPGA 209
 DB 121 CQPCPGTFSSASSSSSQCPHNRCTALGLALNVPSSSDTLCTSCGFPPLSTRVPGA 180
 QY 210 ECERAVIDFAFODISIKRLQRLQALEAPGCGPTPRAGRAALQKLRRRLTELLGAOD 269
 DB 181 ECERAVIDFAFODISIKRLQRLQALEAPGCGPTPRAGRAALQKLRRRLTELLGAOD 240
 QY 270 GALLVRLQALRVARMGELERSVREPLPVH 300
 DB 241 GALLVRLQALRVARMGELERSVREPLPVH 271

RESULT 67

ID AAB19707 standard; Protein: 271 AA.

AC AAB19707;

DT 05-FEB-2001 (first entry)

DE Protease-resistant FLINT analogue R34N, D36T, D194T, S196T, R218Q.

XX FLINT; FAS ligand inhibitory protein; human; protease resistant;

KW acute lung injury; acute respiratory distress syndrome;

KW chronic obstructive pulmonary disease; pulmonary fibrosis;

KW ulcerative colitis; therapy; organ transplantation; substitution;

XX mutant; mutein.

XX Homo sapiens.

XX Synthetic.

FH Key Location/Qualifiers
 FT Misc-difference 34 /note= "Wild-type Arg substituted by Asn"
 FT Misc-difference 194 /note= "Wild-type Asp substituted by Asn"
 FT Misc-difference 196 /note= "Wild-type Ser substituted by Thr"
 FT Misc-difference 36 /note= "Wild-type Asp substituted by Thr"
 FT Misc-difference 218 /note= "Wild-type Arg substituted by Gln"
 FT WO200058466-A2.
 PN
 XX
 PD 05-OCT-2000.
 XX
 PE 20-MAR-2000; 2000WO-US06418.
 XX
 PR 30-MAR-1999; 99US-0126839.
 PR 21-JUN-1999; 99US-0140073.
 PR 04-AUG-1999; 99US-0147071.
 PR 20-OCT-1999; 99US-0160524.
 PR 21-OCT-1999; 99US-0160669.
 PR 20-DEC-1999; 99US-0172744.
 PR 26-JAN-2000; 2000US-0178184.
 PA
 XX (ELIL) LILLY & CO ELI.
 PI Micranovic R, Rathnachalam R, Wlitcher DR;
 DR WPI; 2000-664925/64.
 XX
 PT Novel protease resistant FAS ligand inhibitory protein analogues
 PT resistant to in vivo or in vitro proteolysis at amino acid position 218
 PT of the mature protein, useful for treating autoimmune diseases
 PS Claim 14; Page -; 100pp; English.
 XX
 CC Novel human FLINT analogues are resistant to proteolysis at
 CC position 218 of the wild-type protein (see AAB19705). The present
 CC sequence is a specific example of a protease-resistant FLINT
 CC analogue in which the Arg residue at position 34 has been
 CC substituted by an Asn residue, the Asp residue at position 36 has
 CC been substituted by a Thr residue, the Asp residue at position 194
 CC has been substituted by an Asn residue, the Ser residue at
 CC position 196 has been substituted by a Thr residue, and the Arg
 CC residue at position 218 has been substituted by a Gln residue.
 CC The FLINT analogue can be obtained by mutagenesis of template
 CC FLINT cDNA (see AAB88730) and expressed in recombinant host cells.
 CC It is used to prevent or treat acute lung injury, acute respiratory
 CC stress syndrome, ulcerative colitis, chronic obstructive pulmonary
 CC disease and pulmonary fibrosis. It is also used to inhibit T
 CC lymphocyte activation, to inhibit ischaemic injury during organ
 CC transplantation, and as a component of a liquid medium for
 CC infusion and preservation of organs (claimed). Resistance to
 CC proteolytic cleavage greatly increases in vivo half-life.
 CC Note: The present sequence is not shown in the specification but is
 CC derived from the human FLINT mature protein sequence given in
 CC the Sequence Listing (see AAB19705).
 CC
 XX
 SO Sequence 271 AA;
 Query Match 89.8%; Score 1467; DB 21; Length 271;
 Best Local Similarity 98.2%; Pred. No. 2, 1e-108;
 Matches 266; Conservative 3; Mismatches 2; Indels 0; Gaps 0;

QY 150 COPCPGTFSSASSSSSECCOPHRNCTALGALNVPGSSSHDTCSTGTFPLSTRVPGAE 209
 DB 121 COPCPGTFSSASSSSSECCOPHRNCTALGALNVPGSSSHDTCSTGTFPLSTRVPGAE 180
 QY 210 ECERAVIDFAVFQDISIKRLQRLQALBAPESGWPPTPAGRAALQKLRRLTELLGAD 269
 DB 181 ECERAVIDFAVFQNTTIKRLQRLQALBAPESGWPPTPAGRAALQKLRRLTELLGAD 240
 QY 270 GALLVRLQALRVARMPLERSVRRERFLPVH 300
 DB 241 GALLVRLQALRVARMPLERSVRRERFLPVH 271
 RESULT 68
 ID AAY42185
 AAY42185 standard; Protein; 273 AA.
 AC AAY42185;
 XX
 DT 17-DEC-1999 (first entry)
 XX
 DE Human mFLINT #2 protein sequence.
 XX
 KW Human; FLINT; mFLINT; OPG3; tumour necrosis factor receptor; FasL;
 KW apoptosis; inflammation; cancer; diabetes; acute liver failure;
 KW sepsis; hepatitis; ischemia-associated injury; hypercoagulation;
 KW reperfusion-associated injury; aplastic anaemia; differentiation;
 KW growth; myelodysplastic syndrome; pancytopenic condition;
 KW myocardial ischaemia.
 XX
 OS Homo sapiens.
 XX
 PN WO9950413-A2.
 XX
 PD 07-OCT-1999.
 XX
 PF 30-MAR-1999; 99WO-US06797.
 XX
 PR 30-MAR-1998; 98US-0079856.
 PR 20-MAY-1998; 98US-0086074.
 PR 09-SEP-1998; 98US-0099643.
 PR 17-DEC-1998; 98US-0112577.
 PR 18-DEC-1998; 98US-0112703.
 PR 18-DEC-1998; 98US-0112933.
 PR 22-DEC-1998; 98US-0113407.
 XX
 PA (ELIL) LILLY & CO ELI.
 XX
 PI Bunol TF, Dou S, Glasebrook AL, Gould KE, Hale JE, Heuer JG;
 PI Hui KY, Kharitonkov A, Mizrahi J, Na S, Noblitt TW, Reidy CA;
 PI Song HY, Wang J, Wu X, Zuckerman SH;
 DR WPI; 1999-591319/50.
 DR N-PSDB; AA25378.
 XX
 PT Use of mature FLINT for treating acute liver failure, inflammation,
 PT cancer, and diabetes - by prevention of FasL-Fas mediated apoptotic
 PT and proinflammatory activity
 PT
 PS Example 2; Fig 4; 99pp; English.
 XX
 CC The present invention describes therapeutic applications of mature FLINT
 CC (mFLINT) for use in the treatment of acute liver failure. Mature FLINT
 CC (mFLINT), which is a member of the tumour necrosis factor receptor
 CC superfamily, is used for treating acute liver failure, inflammation of
 CC the liver, abnormal hepatocyte apoptosis, sepsis, a disorder associated
 CC with inflammation, hepatitis, abnormal apoptosis, an ischaemia-associated
 CC injury or disorder such as hypercoagulation (including use with
 CC thrombolytic or anti-thrombolytic agents), reperfusion-associated injury
 CC or disorder, Type I diabetes, cancer, cell damage or damage to an
 CC innocent bystander tissue that is induced by a chemotherapeutic agent or
 CC therapeutic irradiation, treating haematopoietic progenitor cells that

CC have been exposed to therapeutic radiation or chemotherapy, aplastic
 CC anaemia, myelodysplastic syndrome or a pancytopenic condition. mFLINT is
 CC also used for promoting the growth or differentiation of a haematopoietic
 CC progenitor cell or CD34+ cell and preventing damage to a cardiac myocyte
 CC resulting from abnormal myocardial ischaemia. The present sequence
 CC represents human mFLINT.

XX Sequence 273 AA:

Query Match 89.8%; Score 1467; DB 20; Length 273;
 Best Local Similarity 98.5%; Pred. No. 2,1e-108;
 Matches 269; Conservative 0; Mismatches 2; Indels 2; Gaps 1;

OY 30 VAEPTYPWRAETGERLVCAQCPPTGVQRPCCRDSPPTGCPCPRHRYTQFWNYLERCR 89
 DB 1 VAEPTYPWRAETGERLVCAQCPPTGVQRPCCRDSPPTGCPCPRHRYTQFWNYLERCR 60
 OY 90 YCNVLCGEREERARCAHTNRA--CRCRTGFFNAGCLLEHASSPPAGVYARPTSPQN 147
 DB 61 YCNVLCGEREERARCAHTNRA--CRCRTGFFNAGCLLEHASSPPAGVYARPTSPQN 120
 OY 148 TQCCPCPPGTFSASSSSSECCOPHRNCTALGIALNVPSSSHDTLCTCTGFPPLSTRVPG 207
 DB 121 TQCCPCPPGTFSASSSSSECCOPHRNCTALGIALNVPSSSHDTLCTCTGFPPLSTRVPG 180
 OY 208 AEECRRAVIDYAFODISIKRLQRLQALEAPEGMGPPPRAGRAALQIKRRRLTELGA 267
 DB 181 AEECRRAVIDYAFODISIKRLQRLQALEAPEGWAPPRAGRAALQIKRRRLTELGA 240
 OY 268 ODGALLVRLQALRYARMPGLERSYERERFLPVH 300
 DB 241 ODGALLVRLQALRYARMPGLERSYERERFLPVH 273

RESULT 69
 AAY28449
 ID AAY28449 standard; Protein; 245 AA.

XX AAY28449;

DT 29-SEP-1999 (first entry)

DE A human tumour necrosis factor-R2-like proteins (TR2p)-1.

KM Human tumour necrosis factor-R2-like protein; TR2p; achondroplasia;
 KM osteoporosis; developmental disorder; Cushing's syndrome;
 KM muscular dystrophy; epilepsy; hereditary neuropathy;
 KM Charcot-Marie-Tooth disease; neurofibromatosis; hypothyroidism;
 KM hydrocephalus; seizure disorder; cerebral palsy; spinal bifida;
 KM congenital glaucoma; cataract; sensorineural hearing loss;
 KM reproductive disorder; infertility; ovulatory defect; endometriosis;
 KM autoimmune disorder; ectopic pregnancy; teratogenesis; spermatogenesis;
 KM immunological disorder; AIDS; Addison's disease; allergy; bronchitis;
 KM atherosclerosis; diabetes mellitus; Chron's disease; lupus;
 KM irritable bowel syndrome; multiple sclerosis; infection;
 KM neoplastic disorder; adenocarcinoma; leukaemia; lymphoma; melanoma;
 KM myeloma; sarcoma.

KM Homo sapiens.

XX OS

XX PN WO9931128-A2.

XX PD 24-JUN-1999.

XX PF 02-DEC-1998; 98WO-US25649.

XX PR 16-DEC-1997; 97US-0991945.

XX PA (INCYT-) INCYTE PHARM INC.

XX PI Au-Young J, Bandman O, Hillman JL, Kaser MR, Tang YT;
 XX WPI: 1999-457916/38.

DR N-PSDB: AAX89503.

XX New tumour necrosis factor-R2-like protein - useful in the treatment
 PT of osteogenesis, developmental, reproductive, immunological and
 PT neoplastic disorders

XX Claim 1; Fig 1A-C; 81pp; English.

PS The present sequence represents a human tumour necrosis factor-R2-like
 XX protein (TR2p). The protein is used to treat and prevent osteogenesis,
 CC developmental, reproductive, immunological and neoplastic disorders, and
 CC also to diagnose disorders associated with TR2 protein expression. Such
 CC disorders include osteogenesis disorders such as achondroplasia and
 CC osteoporosis, developmental disorders such as Cushing's syndrome,
 CC muscular dystrophy, and epilepsy, hereditary neuropathies such as
 CC Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism,
 CC hydrocephalus, seizure disorders such as cerebral palsy and spinal
 CC bifida, congenital glaucoma, cataract, or sensorineural hearing loss,
 CC reproductive disorders such as infertility, ovulatory defects and
 CC endometriosis, autoimmune disorders, ectopic pregnancy and teratogenesis,
 CC disruption of spermatogenesis, immunological disorders such as AIDS,
 CC Addison's disease, allergies, bronchitis, atherosclerosis, diabetes
 CC mellitus, Chron's disease, lupus and irritable bowel syndrome, multiple
 CC sclerosis, viral, fungal, helminthic, parasitic and protozoal infections,
 CC and neoplastic disorders including adenocarcinoma, leukaemia, lymphoma,
 CC melanoma, myeloma, sarcoma, and teratocarcinoma.

XX Sequence 245 AA:

Query Match 83.4%; Score 1362; DB 20; Length 245;
 Best Local Similarity 99.6%; Pred. No. 4e-100;
 Matches 244; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

OY 1 MRALEGGSLILCLVLAIPALIPYAVAGVAEPTYPWRAETGERLVCAQCPPTGVQVR 60
 DB 1 MRALEGGSLILCLVLAIPALIPYAVAGVAEPTYPWRAETGERLVCAQCPPTGVQVR 60
 OY 61 PCRDSPTTGCPCPPRHRYTQFWNYLERCRVCNVLCGEREERARCAHTNRAKCRGTGF 120
 DB 61 PCRDSPTTGCPCPPRHRYTQFWNYLERCRVCNVLCGEREERARCAHTNRAKCRGTGF 120
 OY 121 AHAGFCLLEHASCPPGACVIAAGPPSONTQCCPCPPGTFSASSSSSECCOPHRNCTALGLA 180
 DB 121 AHAGFCLLEHASCPPGACVIAAGPPSONTQCCPCPPGTFSASSSSSECCOPHRNCTALGLA 180
 OY 181 LNVGSSSHDTLCTCTGFPPLSTRVPAEECEERAVIDFAFODISIKRLQRLQALEAPE 240
 DB 181 LNVGSSSHDTLCTCTGFPPLSTRVPAEECEERAVIDFAFODISIKRLQRLQALEAPE 240
 OY 241 GWGPT 245
 DB 241 DWGPT 245

RESULT 70

AAAB28560
 ID AAB28560 standard; Protein; 211 AA.

XX AAB28560;

DT 08-FEB-2001 (first entry)

DE Human soluble TNF receptor tnfrct-2.

KM Human: tumour necrosis factor like-1; TNF1; tumour necrosis factor; TNF;
 KM immunosuppressive; antirheumatic; neuroprotective; dermatological;
 KM antiinflammatory; antidiabetic; cytostatic; osteopathic; gene therapy;
 KM colon cancer; rheumatoid arthritis; septic shock; Chron's disease;
 KM osteoporosis; autoimmune disease; myasthenia gravis;
 KM insulin-dependent diabetes mellitus.

XX Homo sapiens.

DB 121 PGAECECAVDFVAFODISIKRLQRLQALPAEGKGPTRAGRALQLRRRLTELL 180
OY 266 GAQDQALLVRLQALRVARMPGLERSVEREPLPVH 300
DB 181 GAQDQALLVRLQALRVARMPGLERSVEREPLPVH 215

RESULT 72
AAV22222
ID AAV22222 standard; Protein: 153 AA.
AC AAV22222;
XX
XX
DT 16-SEP-1999 (first entry)
XX
XX
DE Human TNFR superfamily soluble receptor protein sequence.
XX
XX
KW TNFL1: human: TNFR superfamily; tumour necrosis factor ligand; TNF:
KW tumour necrosis factor receptor; TNFR superfamily; cell proliferation;
KW cell differentiation; cytokine production; immunoglobulin; hyperplasia;
KW apoptosis inducer; activated T cell; autoimmune disease; inhibitor;
KW myasthenia gravis; insulin-dependent diabetes mellitus; endotoxin shock;
KW rheumatoid arthritis; multiple sclerosis; systemic lupus erythematosus;
KW tumour; proliferative disorder; neoplasia; dysplasia; immunocompetence;
KW lymphoid organogenesis; bacterial resistance; contact hypersensitivity;
KW delayed type sensitivity; therapy.
XX
XX
OS Homo sapiens.
XX
XX
PN MO9933980-A2.
XX
XX
PD 08-JUL-1999.
XX
XX
PF 22-DEC-1998; 98WO-US27474.
XX
XX
PR 16-DEC-1998; 98US-0212270.
XX
XX
PR 30-DEC-1997; 97US-0068959.
XX
XX
PA (CHIR) CHIRON CORP.
XX
XX
PI Kassam A, Lamson G, Pot D, Tribouley C;
XX
XX
DR WPI: 1999-405508/34.
XX
XX
DR N-PSDB: AAX84621.
XX
XX
PT New tumour necrosis factor ligands, useful for induction of cell
PT death and/or proliferation of cells
XX
XX
PS Claim 1; Page 61; 69pp; English.

This sequence represents a tumour necrosis factor receptor (TNFR) superfamily soluble protein of the invention. The invention also relates to tumour necrosis factor (TNF) ligand (TNFL) family proteins. The TNFL proteins play regulatory roles in cell proliferation and/or differentiation, e.g. they can induce production of cytokines, immunoglobulins, etc. A variety of diseases can be treated by modulating the activity of TNFL proteins, e.g. they can induce apoptosis of activated T cells but rescue resting T cell from apoptosis. TNFL polypeptides can therefore be used to treat autoimmune diseases, such as myasthenia gravis, insulin-dependent diabetes mellitus, rheumatoid arthritis, multiple sclerosis, and systemic lupus erythematosus. TNFL proteins also have tumour stimulating properties, so tumours can be treated by inhibiting the expression or activity of TNFL. Other proliferative disorders, such as neoplasias, dysplasias, and hyperplasia can also be treated using TNFL inhibitors. The TNFL polypeptides and polynucleotides can also be used to enhance or decrease TNF activity, thus providing therapeutic benefits such as induction of cell death, lymphoid organogenesis, or host bacterial resistance, and inhibition of endotoxin shock, contact hypersensitivity, delayed type sensitivity or immunocompetence of a transplant recipient. TNF and its receptors play a major role in host defence and immunosurveillance. As such, there is a need to identify new members of TNFR families. This invention provides this need.

XX
SQ Sequence 153 AA;
Query Match 51.5%; Score 841; DB 20; Length 153;
Best Local Similarity 100.0%; Pred. No. 4.4e-59;
Matches 153; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 85 LERGRYCNVLCGEEREEARACHATHNRACRCRTGFFAHAGFCLFHASCPRGAGVYAGTP 144
DB 1 LERGRYCNVLCGEEREEARACHATHNRACRCRTGFFAHAGFCLFHASCPRGAGVYAGTP 60
OY 145 SONTQOCPPPGTSSASSSSSEOCPPHRCNCTALALANVRSSSHDPLCTSCGTFPRSTR 204
DB 61 SONTQOCPPPGTSSASSSSSEOCPPHRCNCTALALANVRSSSHDPLCTSCGTFPRSTR 120

OY 205 VPGECECAVDFVAFODISIKRLQRLQALE 237
DB 121 VPGECECAVDFVAFODISIKRLQRLQALE 153

RESULT 73
AAB28554
ID AAB28554 standard; protein: 153 AA.
XX
XX
AC AAB28554;
XX
XX
DT 08-FEB-2001 (first entry)
XX
XX
DE Human TNFR soluble receptor #1.
XX
XX
KW Human; tumour necrosis factor like-1; TNFL1; tumour necrosis factor; TNF;
KW immunosuppressive; antiarthritic; neuroprotective; dermatological;
KW antiinflammatory; antidiabetic; cytostatic; osteopathic; gene therapy;
KW colon cancer; rheumatoid arthritis; septic shock; Crohn's disease;
KW osteoporosis; autoimmune disease; myasthenia gravis;
KW insulin-dependent diabetes mellitus.
XX
XX
OS Homo sapiens.
XX
XX
PN WO200060079-A2.
XX
XX
PD 12-OCT-2000.
XX
XX
PF 05-APR-2000; 2000WO-US09058.
XX
XX
PR 05-APR-1999; 99US-0286529.
XX
XX
PA (CHIR) CHIRON CORP.
XX
XX
PI Tribouley C;
XX
XX
DR WPI: 2000-665004/64.
XX
XX
DR N-PSDB: AAC63757.
XX
XX
PT Tumour necrosis factor (TNF) and TNF receptor superfamily protein
PT members TNF-L and TNFR-L, useful for enhancing or decreasing TNF
PT activities such as inducing cell death and lymphoid organogenesis
XX
XX
PS Claim 1; Page 65; 77pp; English.

The present sequence is given in a specification relating to an isolated human protein designated tumour necrosis factor like-1 (TNFL1). It may be used to induce cell death in tumours, to induce apoptosis of activated T cells, to induce inflammation, and to rescue resting T cells from apoptosis. TNF receptors are used to regulate the function of a TNF ligand which plays a role in apoptosis, inflammation, differentiation, or proliferation. Expression of the receptors can also be useful as markers for cancer, especially for colon cancer. Diseases which can be treated using TNFL1 and/or receptors of the TNF/TNFR superfamily include rheumatoid arthritis, cancer, septic shock, Crohn's disease and osteoporosis. The polynucleotides can be used in gene delivery vehicles, for the purpose of delivering a mRNA or oligonucleotide, full-length protein, fusion protein, polypeptide, or ribozyme, or single-chain

CC antibody, into a cell. The newly identified receptor proteins play
 CC regulatory roles in cell proliferation and/or differentiation. The
 CC receptors can also play a role in the negative regulation of
 CC osteoclastogenesis. Soluble TNF-like receptors can be useful in the
 CC neutralisation of TNF or TNF-like ligands. A TNF-L protein can also be
 CC used to treat autoimmune diseases (myasthenia gravis and
 CC insulin-dependent diabetes mellitus), tumours, and proliferative
 CC disorders. A TNF-L or TNFR-L subgenomic polynucleotide can also be
 CC delivered to subjects for the purpose of screening test compounds for
 CC those which are useful for enhancing transfer of TNF-L subgenomic
 CC polynucleotides to the cell or for enhancing subsequent biological
 CC effects of TNF-L or TNFR-L subgenomic polynucleotides within the cell.
 XX
 SQ Sequence 153 AA;

Query Match 51.58; Score 841; DB 21; Length 153;
 Best Local Similarity 100.0%; Pred. No. 4.4e-59;
 Matches 153; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 85 LERCRYCNVLCGEREEARACHATHNRACRCRTGFFAHAGFLEHASCPCGAGYAPGTP 144
 Db 1 LERCRYCNVLCGEREEARACHATHNRACRCRTGFFAHAGFLEHASCPCGAGYAPGTP 144
 QY 145 SONTQOCPCPPGTFSSASSSSSEOCQPHRNCTALGLALNVPGSSHDITCTGTFPLSTR 60
 Db 61 SONTQOCPCPPGTFSSASSSSSEOCQPHRNCTALGLALNVPGSSHDITCTGTFPLSTR 204
 QY 205 VPGAEECERAVIDFAFODISIKRLORLQALE 237
 Db 121 VPGAEECERAVIDFAFODISIKRLORLQALE 153

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